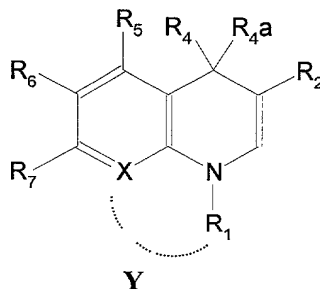


Claims

1. A method for treating a microbial infection in an animal, comprising administering to an animal suffering from said infection an antimicrobial agent and an efflux pump inhibitor in an amount sufficient to reduce efflux pump activity,

wherein said efflux pump inhibitor increases the susceptibility of said microbe to said antimicrobial agent, and

wherein said efflux pump inhibitor has the chemical structure of structure 1 below:



Structure 1

wherein,

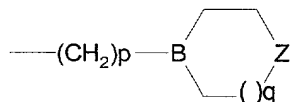
$R_1 =$ H, C_{1-6} alkyl, C_{3-6} cycloalkyl, or optionally substituted aryl, aralkyl, arylaminoalkyl, aryloxyalkyl, arylS(O)_talkyl, where $t=0,1$ or 2 ,
or when X is C and the nitrogen atom to which R_1 is linked forms an optionally substituted 4-, 5-, 6- or 7-membered ring with X of the adjacent ring, the ring optionally containing one or more hetero atoms selected from nitrogen, oxygen or sulfur atoms said heteroatom(s) represented by Y, preferably R_1 is $-CH_2CH_2-$, CH_2Y- , $CH_2CH_2CH_2-$, CH_2CH_2Y- , $CH_2CH_2CH_2CH_2-$ and $CH_2CH_2CH_2Y-$ where Y represents NH, O, or S. If the ring is substituted, the substituent is C_{1-6} alkyl group;

$R_2 =$ H, CHO, COOR₃, or CONHR₁₃,
where $R_{13} =$ H or the NHR₁₃ of CONHR₁₃ is the residue of one of the 20 naturally occurring amino acids: alanine, arginine, asparagines, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine or the optically active isomers thereof or the racemic mixtures thereof, or combinations of these amino acids to give dipeptidyl, tripeptidyl or polypeptidyl residues;

$R_3 =$ H, C_{1-6} alkyl, C_{3-6} cycloalkyl, aryl, aralkyl, arylaminoalkyl, aryloxyalkyl, arylS(O)_talkyl, where $t=0,1$ or 2 ,

$(\text{CH}_2)_n\text{CH}(\text{R}_{14})\text{OC}(=\text{O})\text{R}_{15}$, $(\text{CH}_2)_n\text{CH}(\text{R}_{14})\text{C}(=\text{O})\text{OR}_{15}$ wherein $n = 0-6$, $\text{R}_{14} = \text{H}$ or CH_3 ;
and $\text{R}_{15} = \text{C}_2\text{H}_5$ or $\text{C}(\text{CH}_3)_3$;

or R_3 is



wherein $\text{B}=\text{CH}$ or N , and when $\text{B}=\text{CH}$, $\text{Z}=\text{NH}$ or NCH_3 , and when $\text{B}=\text{N}$, $\text{Z}=\text{CH}$, O , NH , S or NCH_3 ; $p=0-2$; $q=0-2$,

$\text{R}_4 = \text{H}$, $\text{R}_{4a} = \text{H}$, or R_4 and R_{4a} taken together are oxo ($=\text{O}$), or thio ($=\text{S}$);

$\text{R}_5 = \text{H}$, C_{1-5} alkyl, amino, alkylamino, or acylamino;

$\text{R}_6 = \text{H}$, C_{1-6} alkyl, halo, amino, or hydroxy;

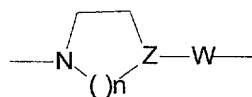
$\text{R}_7 = \text{OH}$, halo or

NR_9 , R_{10} wherein R_9 and R_{10} are the same or different and represent H , C_{1-6} alkyl or $(\text{CH}_2)_n\text{OA}$,

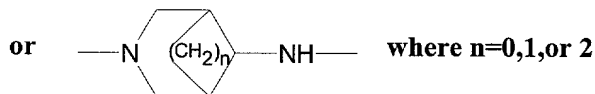
or R_9 is H and R_{10} is a 4-membered, 5-membered, 6-membered, or 7-membered carbocyclic, mono or bicyclic ring or mono or bicyclic heterocyclic ring linked to the nitrogen of NR_9R_{10} through an atom of the heterocycle other than the heterocyclic atom or R_9 and R_{10} taken together with the nitrogen atom to which they are attached form part of a heterocycle which heterocycle is monocyclic, bicyclic, and said carbocycle and heterocycle is optionally substituted;

or $\text{R}_7 = \text{NHOA}$, NHCOOR_{11} , or $\text{NH}(\text{CH}_2)_n\text{NR}_9\text{R}_{10}$;

or $\text{R}_7 =$



where $n=1,2$ or 3 , $\text{Z}=\text{CH}$ or N , and when $\text{Z}=\text{CH}$, $\text{W}=\text{NH}$ or when $\text{Z}=\text{N}$, W is absent;



wherein the R_7 moiety is linked either to 2 core molecules of the Formula I to form a bis compound or the R_7 moiety has one of its link bonds linked to the core formula of Formula I and the second of its link bonds is linked to an optionally substituted phenyl carboxylic acid or ester moiety thereof,

$\text{A} = \text{H}$, C_{1-6} alkyl, glycosyl, aralkyl, C_{1-6} alkanoyl or aminoalkanoyl wherein the aminoalkanoyl group may be an aminoacid residue derived from one of the one of the 20 naturally occurring amino acids or the optically active isomers thereof, or the racemic mixtures thereof wherein the amino residue is derived from alanine, arginine, asparagine, aspartic acid, cysteine, glutamine,

glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine; or.

A is $C_6H_{11}O_6$, SO_3H , or PO_3H_2 ,

$R_{11} = H$, C_{1-6} alkyl, C_{3-6} cycloalkyl, or heterocyclic group,

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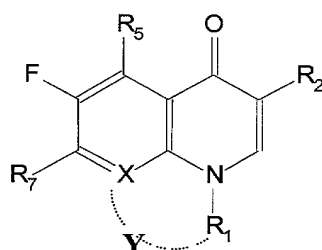
X = CH, C-F, C-Cl, C-CH₃, C-CF₃, C-OCH₃, C-OCHF₂, C-OCF₃, N or when X is equal to C it forms together with the nitrogen atom of the adjacent ring an optionally substituted 5-membered ring, 6-membered ring, 7-membered ring, containing carbon atoms and optionally Y atoms representing one or more nitrogen, oxygen or sulfur atoms; if the ring is substituted, the

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substituent is C_{1-6} alkyl group;
and their pharmaceutically acceptable salts, hydrates, polymorphs and pseudopolymorphs.

2. A method according to claim 1 wherein the efflux pump inhibitor has structure 2

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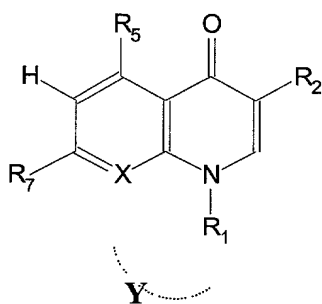
Structure 2

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wherein, R1, R2, R5, R7, X and Y are as defined in claim 1.

3. A method according to claim 1 wherein the efflux pump inhibitor has structure 3

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Structure 3

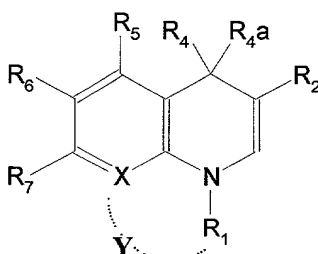
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wherein R1, R2, R5, R7, X and Y are as defined in claim 1.

4. A method for prophylactic treatment of an animal at risk for developing a microbial infection comprising administering to the animal an antimicrobial agent and an efflux pump inhibitor in an amount sufficient to reduce efflux pump activity,

wherein said efflux pump inhibitor increases the susceptibility of said microbe to said antimicrobial agent, and

wherein said efflux pump inhibitor has the chemical structure of structure 1 below:



Structure 1

Wherein,

$R_1 =$ H, C_{1-6} alkyl, C_{3-6} cycloalkyl, or optionally substituted aryl, aralkyl, arylaminoalkyl, aryloxyalkyl,

aryls(O)_talkyl, where $t=0,1$ or 2 ,

or when X is C and the nitrogen atom to which R_1 is linked forms an optionally substituted 4-, 5-, 6- or 7-membered ring with X of the adjacent ring, the ring optionally containing one or more hetero atoms selected from nitrogen, oxygen or sulfur atoms said heteroatom(s) represented by Y, preferably R_1 is $-CH_2CH_2-$, CH_2Y- , $CH_2CH_2CH_2-$, CH_2CH_2Y- , $CH_2CH_2CH_2CH_2-$ and $CH_2CH_2CH_2Y-$ where Y represents NH, O, or S. If the ring is substituted, the substituent is C_{1-6} alkyl group;

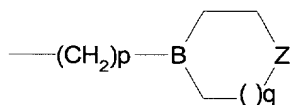
$R_2 =$ H, CHO, COOR₃, or CONHR₁₃,

where $R_{13} =$ H or the NHR₁₃ of CONHR₁₃ is the residue of one of the 20 naturally occurring amino acids: alanine, arginine, asparagines, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine or the optically active isomers thereof or the racemic mixtures thereof, or combinations of these amino acids to give dipeptidyl, tripeptidyl or polypeptidyl residues;

$R_3 =$ H, C_{1-6} alkyl, C_{3-6} cycloalkyl, aryl, aralkyl, arylaminoalkyl, aryloxyalkyl, aryls(O)_talkyl, where $t=0,1$ or 2 ,

$(CH_2)_nCH(R_{14})OC(=O)R_{15}$, $(CH_2)_nCH(R_{14})C(=O)OR_{15}$ wherein $n = 0-6$, $R_{14} =$ H or CH_3 ; and $R_{15} = C_2H_5$ or $C(CH_3)_3$;

or R_3 is



wherein $B=CH$ or N , and when $B=CH$, $Z=NH$ or NCH_3 , and when $B=N$, $Z=CH$, O, NH, S or NCH_3 ; $p=0-2$; $q=0-2$,

$R_4 =$ H, $R_{4a} =$ H, or R_4 and R_{4a} taken together are oxo ($=O$), or thio ($=S$);

$R_5 = H, C_{1-5}$ alkyl, amino, alkylamino, or acylamino;

$R_6 = H, C_{1-6}$ alkyl, halo, amino, or hydroxy;

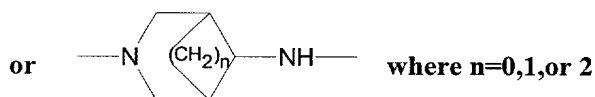
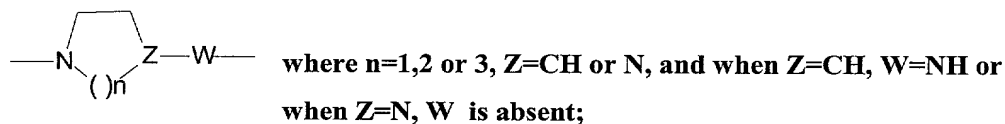
$R_7 = OH$, halo or

NR_9R_{10} wherein R_9 and R_{10} are the same or different and represent H, C_{1-6} alkyl or $(CH_2)_nOA$,

or R_9 is H and R_{10} is a 4-membered, 5-membered, 6-membered, or 7-membered carbocyclic, mono or bicyclic ring or mono or bicyclic heterocyclic ring linked to the nitrogen of NR_9R_{10} through an atom of the heterocycle other than the heterocyclic atom or R_9 and R_{10} taken together with the nitrogen atom to which they are attached form part of a heterocycle which heterocycle is monocyclic, bicyclic, and said carbocycle and heterocycle is optionally substituted;

or $R_7 = NHOA, NHCOOR_{11}$, or $NH(CH_2)_nNR_9R_{10}$;

or $R_7 =$



wherein the R_7 moiety is linked either to 2 core molecules of the Formula I to form a bis compound or the R_7 moiety has one of its link bonds linked to the core formula of Formula I and the second of its link bonds is linked to an optionally substituted phenyl carboxylic acid or ester moiety thereof,

$A = H, C_{1-6}$ alkyl, glycosyl, aralkyl, C_{1-6} alkanoyl or aminoalkanoyl wherein the aminoalkanoyl group may be an aminoacid residue derived from one of the one of the 20 naturally occurring amino acids or the optically active isomers thereof, or the racemic mixtures thereof wherein the amino residue is derived from alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine; or.

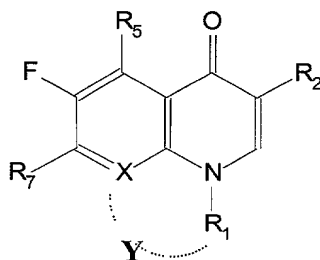
A is $C_6H_{11}O_6, SO_3H$, or PO_3H_2 ,

$R_{11} = H, C_{1-6}$ alkyl, C_{3-6} cycloalkyl, or heterocyclic group,

X = CH, C-F, C-Cl, C-CH₃, C-CF₃, C-OCH₃, C-OCHF₂, C-OCF₃, N or when X is equal to C it forms together with the nitrogen atom of the adjacent ring an optionally substituted 5-membered ring, 6-membered ring, 7-membered ring, containing carbon atoms and optionally Y atoms representing one or more nitrogen, oxygen or sulfur atoms; if the ring is substituted, the substituent is C₁₋₆ alkyl group;

and their pharmaceutically acceptable salts, hydrates, polymorphs and pseudopolymorphs.

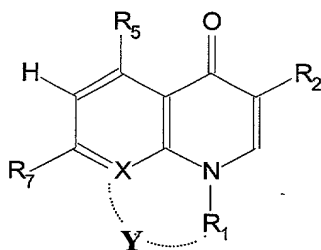
5. A method according to claim 4 wherein the efflux pump inhibitor has structure 2



Structure 2

wherein R1, R2, R5, R7, X and Y are as defined in claim 1.

6. A method according to claim 1 wherein the efflux pump inhibitor has structure 3



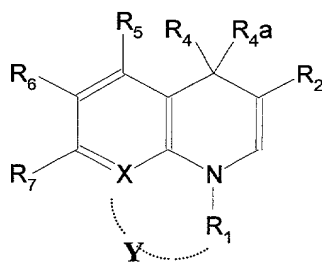
Structure 3

wherein R1, R2, R5, R7, X and Y are as defined in claim 1.

7. The method of any one of claims 1-6 wherein said animal is a mammal.

8. A method of enhancing the antimicrobial activity of an antimicrobial agent against a microbe, comprising contacting said microbe with said antimicrobial agent and an efflux pump inhibitor in an amount effective to inhibit an efflux pump in said microbe,

wherein said efflux pump inhibitor has the chemical structure of structure 1 below:



Structure 1

wherein,

$R_1 =$ H, C_{1-6} alkyl, C_{3-6} cycloalkyl, or optionally substituted aryl, aralkyl, arylaminoalkyl, aryloxyalkyl,

aryls(O)_talkyl, where $t=0,1$ or 2 ,

or when X is C and the nitrogen atom to which R_1 is linked forms an optionally substituted 4-, 5-, 6- or 7-membered ring with X of the adjacent ring, the ring optionally containing one or more hetero atoms selected from nitrogen, oxygen or sulfur atoms said heteroatom(s) represented by Y, preferably R_1 is $-CH_2CH_2-$, CH_2Y- , $CH_2CH_2CH_2-$, CH_2CH_2Y- , $CH_2CH_2CH_2CH_2-$ and $CH_2CH_2CH_2Y-$ where Y represents NH, O, or S. If the ring is substituted, the substituent is C_{1-6} alkyl group;

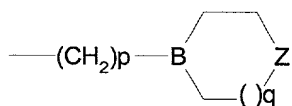
$R_2 =$ H, CHO, $COOR_3$, or $CONHR_{13}$,

where $R_{13} =$ H or the NHR_{13} of $CONHR_{13}$ is the residue of one of the 20 naturally occurring amino acids: alanine, arginine, asparagines, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine or the optically active isomers thereof or the racemic mixtures thereof, or combinations of these amino acids to give dipeptidyl, tripeptidyl or polypeptidyl residues;

$R_3 =$ H, C_{1-6} alkyl, C_{3-6} cycloalkyl, aryl, aralkyl, arylaminoalkyl, aryloxyalkyl, aryls(O)_talkyl, where $t=0,1$ or 2 ,

$(CH_2)_nCH(R_{14})OC(=O)R_{15}$, $(CH_2)_nCH(R_{14})C(=O)OR_{15}$ wherein $n = 0-6$, $R_{14} =$ H or CH_3 ; and $R_{15} = C_2H_5$ or $C(CH_3)_3$;

or R_3 is



wherein $B=CH$ or N , and when $B=CH$, $Z=NH$ or NCH_3 , and when $B=N$, $Z=CH$, O, NH, S or NCH_3 ; $p=0-2$; $q=0-2$,

$R_4 =$ H, $R_{4a} =$ H, or R_4 and R_{4a} taken together are oxo ($=O$), or thio ($=S$);

$R_5 =$ H, C_{1-5} alkyl, amino, alkylamino, or acylamino;

$R_6 =$ H, C_{1-6} alkyl, halo, amino, or hydroxy;

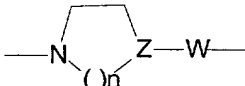
$R_7 =$ OH, halo or

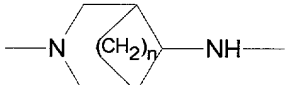
NR_9 , R_{10} wherein R_9 and R_{10} are the same or different and represent H, C_{1-6} alkyl or

$(CH_2)_nOA$,

or R_9 is H and R_{10} is a 4-membered, 5-membered, 6-membered, or 7-membered carbocyclic, mono or bicyclic ring or mono or bicyclic heterocyclic ring linked to the nitrogen of NR_9R_{10} through an atom of the heterocycle other than the heterocyclic atom or R_9 and R_{10} taken together with the nitrogen atom to which they are attached form part of a heterocycle which heterocycle is monocyclic, bicyclic, and said carbocycle and heterocycle is optionally substituted;

or $R_7 = NHOA$, $NHCOOR_{11}$, or $NH(CH_2)_nNR_9R_{10}$;

or $R_7 =$  where $n=1,2$ or 3 , $Z=CH$ or N , and when $Z=CH$, $W=NH$ or when $Z=N$, W is absent;

or  where $n=0,1$, or 2

wherein the R_7 moiety is linked either to 2 core molecules of the Formula I to form a bis compound or the R_7 moiety has one of its link bonds linked to the core formula of Formula I and the second of its link bonds is linked to an optionally substituted phenyl carboxylic acid or ester moiety thereof,

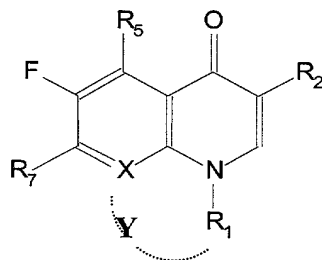
$A = H$, C_{1-6} alkyl, glycosyl, aralkyl, C_{1-6} alkanoyl or aminoalkanoyl wherein the aminoalkanoyl group may be an aminoacid residue derived from one of the one of the 20 naturally occurring amino acids or the optically active isomers thereof, or the racemic mixtures thereof wherein the amino residue is derived from alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine; or.

A is $C_6H_{11}O_6$, SO_3H , or PO_3H_2 ,

$R_{11} = H$, C_{1-6} alkyl, C_{3-6} cycloalkyl, or heterocyclic group,

$X = CH$, $C-F$, $C-Cl$, $C-CH_3$, $C-CF_3$, $C-OCH_3$, $C-OCHF_2$, $C-OCF_3$, N or when X is equal to C it forms together with the nitrogen atom of the adjacent ring an optionally substituted 5-membered ring, 6-membered ring, 7-membered ring, containing carbon atoms and optionally Y atoms representing one or more nitrogen, oxygen or sulfur atoms; if the ring is substituted, the substituent is C_{1-6} alkyl group; and their pharmaceutically acceptable salts, hydrates, polymorphs and pseudopolymorphs.

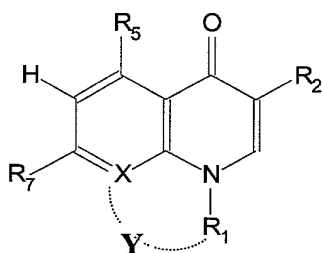
9. The method of claim 8 wherein said efflux pump inhibitor has structure 2



Structure 2

wherein R₁, R₂, R₅, R₇, X and Y are as defined in claim 1.

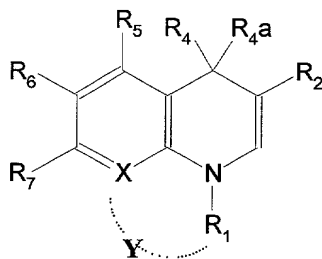
10. A method according to claim 8 wherein the efflux pump inhibitor has structure 3



Structure 3

wherein R₁, R₂, R₅, R₇, X and Y are as defined in claim 1.

11. The method of suppressing growth of a microbe expressing an efflux pump, comprising contacting said microbe with an efflux pump inhibitor in the presence of a concentration of antimicrobial agent below the MIC of said microbe, wherein said efflux pump inhibitor has the chemical structure of structure 1 below:



Structure 1

wherein,

R₁ = H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, or optionally substituted aryl, aralkyl, arylaminoalkyl, aryloxyalkyl, arylS(O)_talkyl, where t=0,1 or 2,

or when X is C and the nitrogen atom to which R₁ is linked forms an optionally substituted 4-, 5-, 6- or 7-membered ring with X of the adjacent ring, the ring optionally containing one or more hetero atoms selected from nitrogen, oxygen or sulfur atoms said heteroatom(s) represented by Y, preferably, R₁ is -CH₂CH₂-,

CH₂Y-, CH₂CH₂CH₂-, CH₂CH₂Y-, CH₂CH₂CH₂CH₂- and CH₂CH₂CH₂Y- where Y represents NH, O, or S. If the ring is substituted, the substituent is C₁₋₆ alkyl group;

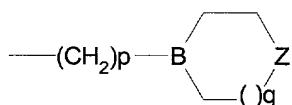
R₂ = H, CHO, COOR₃, or CONHR₁₃,

where R₁₃ = H or the NHR₁₃ of CONHR₁₃ is the residue of one of the 20 naturally occurring amino acids: alanine, arginine, asparagines, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine or the optically active isomers thereof or the racemic mixtures thereof, or combinations of these amino acids to give dipeptidyl, tripeptidyl or polypeptidyl residues;

R₃ = H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, aryl, aralkyl, arylaminoalkyl, aryloxyalkyl, arylS(O)_talkyl, where t=0,1 or 2,

(CH₂)_nCH(R₁₄)OC(=O)R₁₅, (CH₂)_nCH(R₁₄)C(=O)OR₁₅ wherein n = 0-6, R₁₄ = H or CH₃; and R₁₅ = C₂H₅ or C(CH₃)₃;

or R₃ is



wherein B=CH or N, and when B=CH, Z=NH or NCH₃, and when B=N, Z=CH, O, NH, S or NCH₃; p=0-2; q=0-2,

R₄ = H, R_{4a} = H, or R₄ and R_{4a} taken together are oxo (=O), or thio (=S);

R₅ = H, C₁₋₅ alkyl, amino, alkylamino, or acylamino;

R₆ = H, C₁₋₆ alkyl, halo, amino, or hydroxy;

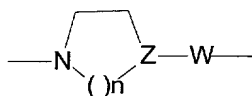
R₇ = OH, halo or

NR₉ R₁₀ wherein R₉ and R₁₀ are the same or different and represent H, C₁₋₆ alkyl or (CH₂)_nOA,

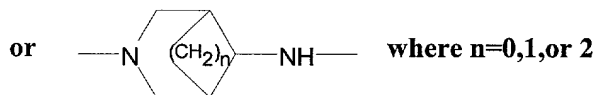
or R₉ is H and R₁₀ is a 4-membered, 5-membered, 6-membered, or 7-membered carbocyclic, mono or bicyclic ring or mono or bicyclic heterocyclic ring linked to the nitrogen of NR₉R₁₀ through an atom of the heterocycle other than the heterocyclic atom or R₉ and R₁₀ taken together with the nitrogen atom to which they are attached form part of a heterocycle which heterocycle is monocyclic, bicyclic, and said carbocycle and heterocycle is optionally substituted;

or R₇ = NHOA, NHCOOR₁₁, or NH(CH₂)_nNR₉R₁₀;

or R₇ =



where n=1,2 or 3, Z=CH or N, and when Z=CH, W=NH or when Z=N, W is absent;



wherein the R₇ moiety is linked either to 2 core molecules of the Formula I to form a bis compound or the R₇ moiety has one of its link bonds linked to the core formula of Formula I and the second of its link bonds is linked to an optionally substituted phenyl carboxylic acid or ester moiety thereof,

A = H, C₁₋₆ alkyl, glycosyl, aralkyl, C₁₋₆ alkanoyl or aminoalkanoyl wherein the aminoalkanoyl group may be an aminoacid residue derived from one of the one of the 20 naturally occurring amino acids or the optically active isomers thereof, or the racemic mixtures thereof wherein the amino residue is derived from alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine; or.

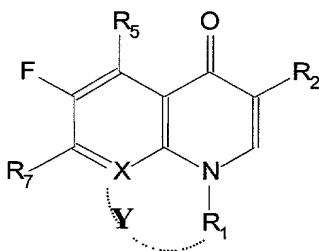
A is C₆H₁₁O₆, SO₃H, or PO₃H₂,

R₁₁ = H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, or heterocyclic group,

X = CH, C-F, C-Cl, C-CH₃, C-CF₃, C-OCH₃, C-OCHF₂, C-OCF₃, N or when X is equal to C it forms together with the nitrogen atom of the adjacent ring an optionally substituted 5-membered ring, 6-membered ring, 7-membered ring, containing carbon atoms and optionally Y atoms representing one or more nitrogen, oxygen or sulfur atoms; if the ring is substituted, the substituent is C₁₋₆ alkyl group;

and their pharmaceutically acceptable salts, hydrates, polymorphs and pseudopolymorphs.

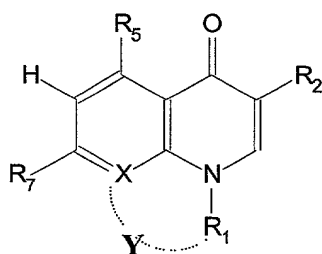
12.The method of claim 11 wherein said efflux pump inhibitor has structure 2



Structure 2

wherein R₁, R₂, R₅, R₇, X and Y are as defined in claim 1.

13. A method according to claim 11 wherein the efflux pump inhibitor has structure 3



Structure 3

wherein R1, R2, R5, R7, X and Y are as defined in claim 1

14. The method of any one of claims 11 to 13, wherein said efflux pump is a Mef A or MefE pump.

15. The method of any one of claims 11 to 13, wherein said efflux pump is a NorA, Bmr, PmrA or QacA or QcaB pump.

16. The method of any one of claims 11 to 13, wherein said microbe expressing an efflux pump is a Gram negative organism-bearing MexAB-OprM, MexCD-OprJ, MexEF-OprM, MexXY-OprM, ARcrAB-TolC, AcrEF, MarA, SoxS, or/and Tet pump/s.

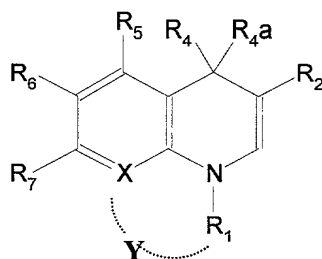
17. The method of any one of claims 1 to 16, wherein said microbe is a bacterium.

18. The method of claim 17, wherein said bacterium is selected from the group consisting of *Pseudomonas aeruginosa*, *Pseudomonas fluorescens*, *Pseudomonas acidovorans*, *Pseudomonas alcaligenes*, *Pseudomonas putida*, *Stenotrophomonas maltophilia*, *Burkholderia cepacia*, *Burkholderia pseudomallei*, *Aeromonas hydrophilia*, *Escherichia coli*, *Citrobacter freundii*, *Salmonella typhimurium*, *Salmonella enterica* Serovar *typhimurium*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella enteritidis*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Enterobacter cloacae*, *Enterobacter aerogenes*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Serratia marcescens*, *Francisella tularensis*, *Morganella morganii*, *Proteus mirabilis*, *Proteus vulgaris*, *Providencia alcalifaciens*, *Providencia rettgeri*, *Providencia stuartii*, *Acinetobacter calcoaceticus*, *Acinetobacter haemolyticus*, *Yersinia enterocolitica*, *Yersinia pestis*, *Yersinia pseudotuberculosis*, *Yersinia intermedia*, *Bordetella pertussis*, *Bordetella parapertussis*, *Bordetella bronchiseptica*, *Haemophilus influenzae*, *Haemophilus parainfluenzae*, *Haemophilus haemolyticus*, *Haemophilus parahaemolyticus*, *Haemophilus ducreyi*, *Pasteurella multocida*, *Pasteurella haemolytica*, *Branhamella catarrhalis*, *Helicobacter pylori*, *Campylobacter fetus*, *Campylobacter jejuni*, *Campylobacter coli*, *Borrelia burgdorferi*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Legionella pneumophila*, *Listeria monocytogenes*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Gardnerella vaginalis*, *Bacteroides fragilis*, *Bacteroides distasonis*, *Bacteroides 3452A* homology group, *Bacteroides vulgatus*, *Bacteroides ovalus*, *Bacteroides thetaiotaomicron*, *Bacteroides uniformis*, *Bacteroides eggerthii*, *Bacteroides splanchnicus*, *Clostridium difficile*, *Mycobacterium tuberculosis*, *Mycobacterium avium*, *Mycobacterium intracellulare*, *Mycobacterium leprae*, *Corynebacterium diphtheriae*, *Corynebacterium ulcerans*, *Streptococcus pneumoniae*, *Streptococcus agalactiae*, *Streptococcus pyogenes*, *Enterococcus faecalis*, *Enterococcus faecium* and *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus saprophyticus*, *Staphylococcus intermedius*, *Staphylococcus hyicus* subsp. *hyicus*, *Staphylococcus haemolyticus*, *Staphylococcus hominis*, and *Rickettsia prowazekii*.

19. The method of claim 18, wherein said bacterium is selected from the group consisting of *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Pseudomonas aeruginosa*, *Escherichia coli*,

and *Staphylococcus aureus*.

20. The method of any one of claims 1 to 19 wherein said microbial infection is a bacterial infection and said antimicrobial agent is an antibacterial agent.
21. The method of claim 20, wherein said antibacterial agent is a quinolone.
22. The method of claim 20, wherein said antibacterial agent is a tetracycline.
23. The method of claim 20, wherein said antibacterial agent is a beta-lactam.
24. The method of claim 20, wherein said antibacterial agent is a coumermycin.
25. The method of claim 20, wherein said antibacterial agent is chloramphenicol.
26. The method of claim 20, wherein said antibacterial agent is a glycopeptide.
27. The method of claim 20, wherein said antibacterial agent is an aminoglycoside.
28. The method of claim 20, wherein said antibacterial agent is a macrolide.
29. The method of claim 20, wherein said antibacterial agent is a rifamycin.
30. The method of claim 20, wherein said antibacterial agent is an oxazolidonone.
31. The method of any of claims 1, 4, 8 or 11 wherein said antimicrobial agent is effluxed by a microbe.
32. An efflux inhibitor compound, wherein said compound has the chemical structure 1 below:



Structure 1

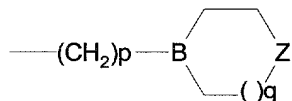
wherein,

- $R_1 =$ H, C_{1-6} alkyl, C_{3-6} cycloalkyl, or optionally substituted aryl, aralkyl, arylaminoalkyl, aryloxyalkyl, arylS(O)_talkyl, where $t=0,1$ or 2 , or when X is C and the nitrogen atom to which R_1 is linked forms an optionally substituted 4-, 5-, 6- or 7-membered ring with X of the adjacent ring, the ring optionally containing one or more hetero atoms selected from nitrogen, oxygen or sulfur atoms said heteroatom(s) represented by Y, preferably R_1 is $-CH_2CH_2-$, CH_2Y- , $CH_2CH_2CH_2-$, CH_2CH_2Y- , $CH_2CH_2CH_2CH_2-$ and $CH_2CH_2CH_2Y-$ where Y represents NH, O, or S. If the ring is substituted, the substituent is C_{1-6} alkyl group;
- $R_2 =$ H, CHO, COOR₃, or CONHR₁₃, where $R_{13} =$ H or the NHR₁₃ of CONHR₁₃ is the residue of one of the 20 naturally occurring amino acids: alanine, arginine, asparagines, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine or the optically active isomers

thereof or the racemic mixtures thereof, or combinations of these amino acids to give dipeptidyl, tripeptidyl or polypeptidyl residues;

$R_3 =$ H, C_{1-6} alkyl, C_{3-6} cycloalkyl, aryl, aralkyl, arylaminoalkyl, aryloxyalkyl, arylS(O)_talkyl, where $t=0,1$ or 2 ,
(CH_2)_nCH(R_{14})OC(=O) R_{15} , (CH_2)_nCH(R_{14})C(=O)OR₁₅ wherein $n = 0-6$, $R_{14} = H$ or CH_3 ;
and $R_{15} = C_2H_5$ or $C(CH_3)_3$;

or R_3 is



wherein $B=CH$ or N , and when $B=CH$, $Z=NH$ or NCH_3 , and when $B=N$, $Z=CH$, O , NH , S or NCH_3 ; $p=0-2$; $q=0-2$,

$R_4 =$ H, $R_{4a} = H$, or R_4 and R_{4a} taken together are oxo ($=O$), or thio ($=S$);

$R_5 =$ H, C_{1-5} alkyl, amino, alkylamino, or acylamino;

$R_6 =$ H, C_{1-6} alkyl, halo, amino, or hydroxy;

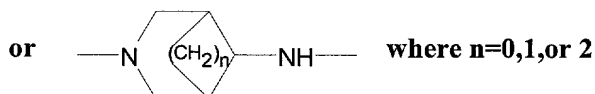
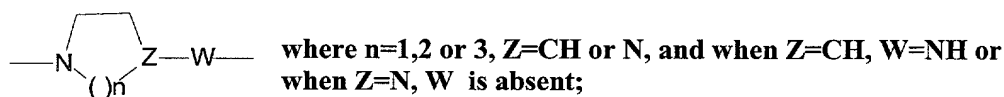
$R_7 = OH$, halo or

NR_9R_{10} wherein R_9 and R_{10} are the same or different and represent H, C_{1-6} alkyl or $(CH_2)_nOA$,

or R_9 is H and R_{10} is a 4-membered, 5-membered, 6-membered, or 7-membered carbocyclic, mono or bicyclic ring or mono or bicyclic heterocyclic ring linked to the nitrogen of NR_9R_{10} through an atom of the heterocycle other than the heterocyclic atom or R_9 and R_{10} taken together with the nitrogen atom to which they are attached form part of a heterocycle which heterocycle is monocyclic, bicyclic, and said carbocycle and heterocycle is optionally substituted;

or $R_7 = NHOA$, $NHCOOR_{11}$, or $NH(CH_2)_nNR_9R_{10}$;

or $R_7 =$



wherein the R_7 moiety is linked either to 2 core molecules of the Formula I to form a bis compound or the R_7 moiety has one of its link bonds linked to the core formula of Formula I and the second of its link bonds is linked to an optionally substituted phenyl carboxylic acid or ester moiety thereof,

$A =$ H, C_{1-6} alkyl, glycosyl, aralkyl, C_{1-6} alkanoyl or aminoalkanoyl wherein the aminoalkanoyl group may be an aminoacid residue derived from one of the one of the 20 naturally occurring amino acids or the optically active isomers thereof, or the racemic mixtures thereof wherein the amino residue is derived from alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine; or.

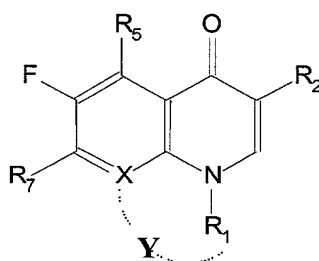
A is $C_6H_{11}O_6$, SO_3H , or PO_3H_2 ,

$R_{11} = \text{H, C}_{1-6} \text{ alkyl, C}_{3-6} \text{ cycloalkyl, or heterocyclic group,}$

$X = \text{CH, C-F, C-Cl, C-CH}_3, \text{C-CF}_3, \text{C-OCH}_3, \text{C-OCHF}_2, \text{C-OCF}_3, \text{N}$ or when X is equal to C it forms together with the nitrogen atom of the adjacent ring an optionally substituted 5-membered ring, 6-membered ring, 7-membered ring, containing carbon atoms and optionally Y atoms representing one or more nitrogen, oxygen or sulfur atoms; if the ring is substituted, the substituent is C_{1-6} alkyl group;

and their pharmaceutically acceptable salts, hydrates, polymorphs and pseudopolymorphs.

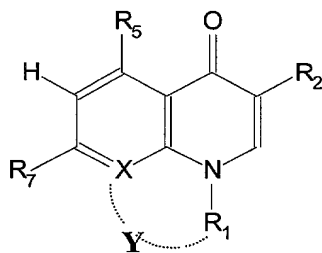
33. An efflux inhibitor compound according to claim 32, wherein said compound has the chemical structure 2 below



Structure 2

wherein R_1, R_2, R_5, R_7, X and Y are as defined in claim 1.

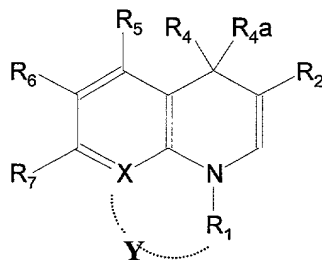
34. An efflux inhibitor compound according to claim 32, wherein said compound has the chemical structure 3 below



Structure 3

wherein R_1, R_2, R_5, R_7, X and Y are as defined in claim 1.

35. An efflux pump inhibitor of the Mef pump wherein said efflux pump inhibitor has the Structure 1 below



Structure 1

wherein,

$R_1 =$ H, C_{1-6} alkyl, C_{3-6} cycloalkyl, or optionally substituted aryl, aralkyl, arylaminoalkyl, aryloxyalkyl,

arylS(O)_talkyl, where $t=0,1$ or 2 ,

or when X is C and the nitrogen atom to which R_1 is linked forms an optionally substituted 4-, 5-, 6- or 7-membered ring with X of the adjacent ring, the ring optionally containing one or more hetero atoms selected from nitrogen, oxygen or sulfur atoms said heteroatom(s) represented by Y, preferably R_1 is $-CH_2CH_2-$, CH_2Y- , $CH_2CH_2CH_2-$, CH_2CH_2Y- , $CH_2CH_2CH_2CH_2-$ and $CH_2CH_2CH_2Y-$ where Y represents NH, O, or S. If the ring is substituted, the substituent is C_{1-6} alkyl group;

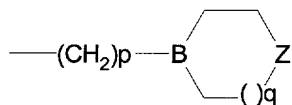
$R_2 =$ H, CHO, COOR₃, or CONHR₁₃,

where $R_{13} =$ H or the NHR₁₃ of CONHR₁₃ is the residue of one of the 20 naturally occurring amino acids: alanine, arginine, asparagines, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine or the optically active isomers thereof or the racemic mixtures thereof, or combinations of these amino acids to give dipeptidyl, tripeptidyl or polypeptidyl residues;

$R_3 =$ H, C_{1-6} alkyl, C_{3-6} cycloalkyl, aryl, aralkyl, arylaminoalkyl, aryloxyalkyl, arylS(O)_talkyl, where $t=0,1$ or 2 ,

$(CH_2)_nCH(R_{14})OC(=O)R_{15}$, $(CH_2)_nCH(R_{14})C(=O)OR_{15}$ wherein $n = 0-6$, $R_{14} =$ H or CH_3 ; and $R_{15} = C_2H_5$ or $C(CH_3)_3$;

or R_3 is



wherein $B=CH$ or N , and when $B=CH$, $Z=NH$ or NCH_3 , and when $B=N$, $Z=CH$, O, NH, S or NCH_3 ; $p=0-2$; $q=0-2$,

$R_4 =$ H, $R_{4a} =$ H, or R_4 and R_{4a} taken together are oxo ($=O$), or thio ($=S$);

$R_5 =$ H, C_{1-5} alkyl, amino, alkylamino, or acylamino;

$R_6 =$ H, C_{1-6} alkyl, halo, amino, or hydroxy;

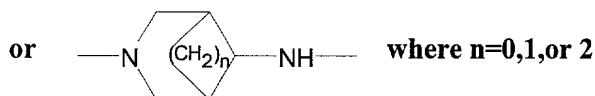
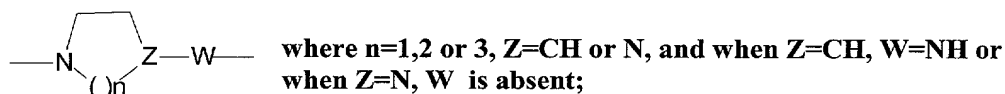
$R_7 = \text{OH}$, halo or

NR_9R_{10} wherein R_9 and R_{10} are the same or different and represent H, C_{1-6} alkyl or $(\text{CH}_2)_n\text{OA}$,

or R_9 is H and R_{10} is a 4-membered, 5-membered, 6-membered, or 7-membered carbocyclic, mono or bicyclic ring or mono or bicyclic heterocyclic ring linked to the nitrogen of NR_9R_{10} through an atom of the heterocycle other than the heterocyclic atom or R_9 and R_{10} taken together with the nitrogen atom to which they are attached form part of a heterocycle which heterocycle is monocyclic, bicyclic, and said carbocycle and heterocycle is optionally substituted;

or $R_7 = \text{NHOA}$, NHCOOR_{11} , or $\text{NH}(\text{CH}_2)_n\text{NR}_9\text{R}_{10}$;

or $R_7 =$



wherein the R_7 moiety is linked either to 2 core molecules of the Formula I to form a bis compound or the R_7 moiety has one of its link bonds linked to the core formula of Formula I and the second of its link bonds is linked to an optionally substituted phenyl carboxylic acid or ester moiety thereof,

$A = \text{H}$, C_{1-6} alkyl, glycosyl, aralkyl, C_{1-6} alkanoyl or aminoalkanoyl wherein the aminoalkanoyl group may be an aminoacid residue derived from one of the one of the 20 naturally occurring amino acids or the optically active isomers thereof, or the racemic mixtures thereof wherein the amino residue is derived from alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine; or.

A is $\text{C}_6\text{H}_{11}\text{O}_6$, SO_3H , or PO_3H_2 ,

$R_{11} = \text{H}$, C_{1-6} alkyl, C_{3-6} cycloalkyl, or heterocyclic group,

$X = \text{CH}$, C-F , C-Cl , C-CH_3 , C-CF_3 , C-OCH_3 , C-OCHF_2 , C-OCF_3 , N or when X is equal to C it forms together with the nitrogen atom of the adjacent ring an optionally substituted 5-membered ring, 6-membered ring, 7-membered ring, containing carbon atoms and optionally Y atoms representing one or more nitrogen, oxygen or sulfur atoms; if the ring is substituted, the substituent is C_{1-6} alkyl group; and their pharmaceutically acceptable salts, hydrates, polymorphs and pseudopolymorphs.

36. The efflux pump inhibitor according to claim 35 selected from:

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-amino-3'-methyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-{4'-(methylamino)-3',3'-dimethylpiperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

i-Propyl 1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-amino-3',3'-dimethyl-piperidin-1-yl)-4-oxo-quinoline-3-carboxylate and its salts;

n-Butyl 1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-amino-3',3'-dimethyl-piperidin-1-yl)-4-oxo-quinoline-3-carboxylate and its salts;

Ethoxycarbonylmethyl 1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-amino-3',3'-dimethylpiperidin-1-yl)-4-oxo-quinoline-3-carboxylate and its salts;

Benzyl 1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-{4'-(t-butoxycarbonyl amino)-3',3'-dimethylpiperidin-1-yl}-4-oxo-quinoline-3-carboxylate and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-{4'-N-(t-butoxycarbonyl-L-alanyl) amino-3',3'-dimethylpiperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid hydrochloride;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-L-alanylamino-3',3'-dimethylpiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid hydrochloride;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(3',3'-dimethyl-4'-(t-butoxycarbonylvalinylamino)piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(3',3'-dimethyl-4'-(L)-valyl-aminopiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid hydrochloride;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-{4'-(L)-aspartylamino-3',3'-dimethylpiperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid hydrochloride;

1-Ethyl-6,8-difluoro-1,4-dihydro-7-(4'-ethylaminopiperidin-1'-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6,8-difluoro-1,4-dihydro-7-(4'-amino-3'-methyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6,8-difluoro-1,4-dihydro-7-(quinuclidinyl-3-yl-amino)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6,8-difluoro-1,4-dihydro-7-{(1 α ,5 α ,6 α)-6-amino-N-benzyl-3-azabicyclo[3.1.0] hex-6-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

1-(3'-Fluorophenyl)-6-fluoro-1,4-dihydro-7-(4'-methylpiperazin-1'-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-(2,4-Difluorophenyl)-6-fluoro-1,4-dihydro-7-(4'-ethylaminopiperidin-1'-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-(2',4'-Difluorophenyl)-6-fluoro-5-methyl-1,4-dihydro-7-(4'-aminopiperidin-1'-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-(2',4'-Difluorophenyl)-6-fluoro-5-methyl-1,4-dihydro-7-(4'-methylamino piperidin-1'-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1,4-dihydro-7-(3'-aminopyrrolidin-1'-yl)-4-oxo-1,8-naphthyridine-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1,4-dihydro-7-((1 α ,5 α ,6 α)-6-amino--N-benzyl-3-azabicyclo [3.1.0] hex-6-yl)-4-oxo-1,8-naphthyridine-3-carboxylic acid and its salts;

1-(2,4-Difluorophenyl) -6-fluoro-1, 4-dihydro-7-(3'-aminopyrrolidin-1'-yl)- 4-oxo-1,8-naphthyridine-3-carboxylic acid and its salts;

1-(2,4-Difluorophenyl) -6-fluoro-1, 4-dihydro-7-((1 α ,5 α ,6 α)-6-amino-N-benzyl-3-azabicyclo [3.1.0]hex-6-yl)- 4-oxo-1,8-naphthyridine-3-carboxylic acid and its salts;

1-(2,4-Difluorophenyl)-6-fluoro-1,4-dihydro-7-(3',3'-dimethyl-4'-hydroxy piperdin-1'-yl)-4-oxo-1,8-naphthyridine-3-carboxylic acid and its salts;

(RS)-(±)-9-Fluoro-6, 7-dihydro-8-{4'-(L- α -aspartoxy)piperidin-1-yl}-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid hydrochloride;

7H-Pyrido[1,2,3-de]-1,4-benzoxazine-9-fluoro-2,3-dihydro-3-methyl-10-(3'-ethyl 4'-hydroxypiperidin-1'-yl)-7-oxo-6-carboxylic acid and its salts;

7H-Pyrido[1,2,3-de]-1,4-benzoxazine-9-fluoro-2, 3-dihydro-3-methyl-10- (3'-amino methyl-4'-hydroxypiperidin-1'-yl)-7-oxo-6-carboxylic acid and its salt;

1-Cyclopropyl-6, 8-difluoro-5-methyl-1, 4-dihydro -7-(3', 3'-dimethyl-4'-ethylamino piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salt;

1-Cyclopropyl-6,7,8-trifluoro-5-methyl-1,4-dihydro - 4-oxo-quinoline-3-carboxylic acid;

(S)-(-)-9-Fluoro-6,7-dihydro-8- (3', 3'-dimethyl-4'-ethylaminopiperidin-1-yl)-5-methyl-1-oxo-1H, 5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro-7- (3'-aminomethyl-4'-hydroxypiperidin 1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro-7- (4'-dimethylamino-3'-methylpiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-{4'-cyclopropyl aminopiperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1, 4-dihydro -7-(4'-(t-butoxycarbonyl (L)-Ala-Ala)amino-3', 3'-dimethyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid hydrochloride;

5-Amino-1-cyclopropyl-6-fluoro-8-methoxy-1, 4-dihydro -7-{4'-ethylamino-3', 5'-dimethylpiperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

Ethyl 1-(2,4-difluorophenyl) -6-fluoro -1, 4-dihydro-7- (4-amino-3-ethylpiperidin-1-yl)- 4-oxo-1,8-naphthyridine-3-carboxylate;

1-(2,4-difluorophenyl) -6-fluoro-1, 4-dihydro-7- (4-amino-3, 5-dimethylpiperidin-1-yl)- 4-oxo-1,8-naphthyridine-3-carboxylic acid and its salts;

Ethyl 1-(2,4-difluorophenyl)-6-fluoro-5-methyl-1,4-dihydro-7-(4-amino-3,3-dimethylpiperidin-1-yl)-4-oxo-1,8-naphthyridine-3-carboxylate;

(S)-(-)-9-fluoro-6,7-dihydro-8-(4'-hydroxy-3'-fluoropiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts;

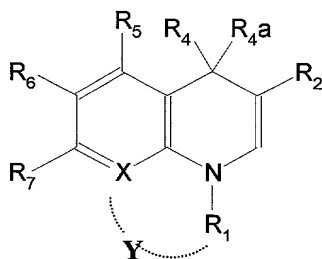
10-Fluoro-11-(4-aminopiperidin-1-yl)-3,4-dihydro-4(S)-methyl-8-oxo-2H,8H-pyrido[1,2,3-ef]-1,5-benzoxazipin-7-carboxylic acid and its salt;

(RS)-(±)-6,7-dihydro-8-(trans-4'-hydroxy-3'-methylpiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts;

(RS)-(±)-6,7-dihydro-8-(cis-4'-hydroxy-3'-methylpiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts; or

(RS)-(±)-6,7-dihydro-8-(4'-hydroxy-3',3'-dimethylpiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts.

37. An efflux pump inhibitor of the NorA, Bmr, PmrA, QacA and/or QacB pump/s wherein said efflux pump inhibitor has the Structure 1 below



Structure 1

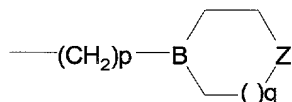
wherein,

$R_1 =$ H, C_{1-6} alkyl, C_{3-6} cycloalkyl, or optionally substituted aryl, aralkyl, arylaminoalkyl, aryloxyalkyl, $arylS(O)_t$ alkyl, where $t=0,1$ or 2 ,
or when X is C and the nitrogen atom to which R_1 is linked forms an optionally substituted 4-, 5-, 6- or 7-membered ring with X of the adjacent ring, the ring optionally containing one or more hetero atoms selected from nitrogen, oxygen or sulfur atoms said heteroatom(s) represented by Y, preferably R_1 is $-CH_2CH_2-$, CH_2Y- , $CH_2CH_2CH_2-$, CH_2CH_2Y- , $CH_2CH_2CH_2CH_2-$ and $CH_2CH_2CH_2Y-$ where Y represents NH, O, or S. If the ring is substituted, the substituent is C_{1-6} alkyl group;

$R_2 =$ H, CHO, $COOR_3$, or $CONHR_{13}$,
where $R_{13} =$ H or the NHR_{13} of $CONHR_{13}$ is the residue of one of the 20 naturally occurring amino acids: alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine or the optically active isomers thereof or the racemic mixtures thereof, or combinations of these amino acids to give dipeptidyl, tripeptidyl or polypeptidyl residues;

$R_3 =$ H, C_{1-6} alkyl, C_{3-6} cycloalkyl, aryl, aralkyl, arylaminoalkyl, aryloxyalkyl, $arylS(O)_t$ alkyl, where $t=0,1$ or 2 ,
 $(CH_2)_nCH(R_{14})OC(=O)R_{15}$, $(CH_2)_nCH(R_{14})C(=O)OR_{15}$ wherein $n = 0-6$, $R_{14} =$ H or CH_3 ;
and $R_{15} = C_2H_5$ or $C(CH_3)_3$;

or R_3 is



wherein B=CH or N, and when B=CH, Z=NH or NCH₃, and when B=N, Z=CH, O, NH, S or NCH₃; p=0-2; q=0-2,

R₄ = H, R_{4a} = H, or R₄ and R_{4a} taken together are oxo (=O), or thio (=S);

R₅ = H, C₁₋₅ alkyl, amino, alkylamino, or acylamino;

R₆ = H, C₁₋₆ alkyl, halo, amino, or hydroxy;

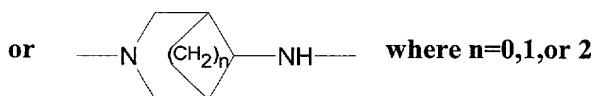
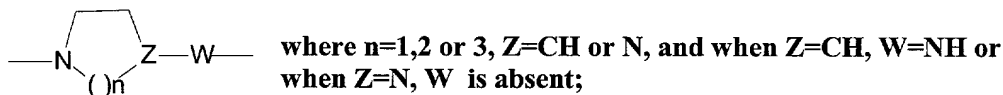
R₇ = OH, halo or

NR₉R₁₀ wherein R₉ and R₁₀ are the same or different and represent H, C₁₋₆ alkyl or (CH₂)_nOA,

or R₉ is H and R₁₀ is a 4-membered, 5-membered, 6-membered, or 7-membered carbocyclic, mono or bicyclic ring or mono or bicyclic heterocyclic ring linked to the nitrogen of NR₉R₁₀ through an atom of the heterocycle other than the heterocyclic atom or R₉ and R₁₀ taken together with the nitrogen atom to which they are attached form part of a heterocycle which heterocycle is monocyclic, bicyclic, and said carbocycle and heterocycle is optionally substituted;

or R₇ = NHOA, NHCOOR₁₁, or NH(CH₂)_nNR₉R₁₀;

or R₇ =



wherein the R₇ moiety is linked either to 2 core molecules of the Formula I to form a bis compound or the R₇ moiety has one of its link bonds linked to the core formula of Formula I and the second of its link bonds is linked to an optionally substituted phenyl carboxylic acid or ester moiety thereof,

A = H, C₁₋₆ alkyl, glycosyl, aralkyl, C₁₋₆ alkanoyl or aminoalkanoyl wherein the aminoalkanoyl group may be an aminoacid residue derived from one of the one of the 20 naturally occurring amino acids or the optically active isomers thereof, or the racemic mixtures thereof wherein the amino residue is derived from alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine; or.

A is C₆H₁₁O₆, SO₃H, or PO₃H₂,

R₁₁ = H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, or heterocyclic group,

X = CH, C-F, C-Cl, C-CH₃, C-CF₃, C-OCH₃, C-OCHF₂, C-OCF₃, N or when X is equal to C it forms together with the nitrogen atom of the adjacent ring an optionally substituted 5-membered ring, 6-membered ring, 7-membered ring, containing carbon atoms and optionally Y atoms representing one or more nitrogen, oxygen or sulfur atoms; if the ring is substituted, the substituent is C₁₋₆ alkyl group;

and their pharmaceutically acceptable salts, hydrates, polymorphs and pseudopolymorphs.

38. The efflux pump inhibitor according to claim 37 selected from :

1-Ethyl-6-fluoro-1, 4-dihydro -7-(1', 2', 3', 4'-tetrahydroisoquinolin-2-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Ethyl-6,8-fluoro-1, 4-dihydro -7-(4'-acetoxypiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Ethyl-6,8-fluoro-1, 4-dihydro -7-(4'-(2'-(2'-oxazolidin-1-yl) ethyl) piperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1- Ethyl-6, 8-difluoro-1, 4-dihydro -7-((1 α ,5 α ,6 α)-6-amino-3-azabicyclo [3.1.0]-hex-3-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1- ethyl -6, 8-difluoro-1, 4-dihydro -7-(3'-amino-5'-methyl pyrrolidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1- ethyl-6, 8-difluoro-1, 4-dihydro -7-(4'-aminopiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1- ethyl -6, 8-difluoro-1, 4-dihydro -7-{4'-(acetamido) piperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1- ethyl-6, 8-difluoro-1, 4-dihydro -7-((1 α ,5 α ,6 α)-6'-(t-butoxycarbonyl amino)-3-azabicyclo [3.1.0]-hex-3-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro-7-(3'-acetamido-5'-methylpyrrolidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro-7-(3'-amino-5'-methylpyrrolidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1,4-dihydro-7-(4'-acetoxypiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1,4-dihydro -7-{4'-(dimethylamino) piperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1,4-dihydro-7-(3',5'-dimethylpiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro -7-(4'-hydroxy-3',5'-dimethylpiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro- -7-(3', 4', 5'-trimethyl piperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro- 7-(3', 5'-dimethyl-4'-ethyl piperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro-5-methyl- 7-(4'-ethoxypiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro-5-methyl- 7-(3', 3'-dimethylpiperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-{4'-(dimethylamino)-3'-methyl piperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-hydroxy-3'-isobutyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-hydroxy-3',3'-dimethyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-hydroxy-3',5'-dimethyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(3'-methylpiperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(cis-4'-amino-3',5'-dimethylpiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6,8-difluoro-5-methyl-1,4-dihydro-7-(4'-hydroxy-3'-aminomethyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6,8-difluoro-1,4-dihydro-7-(5'amino-2'-methyl-pyrrolidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro -7-{3'-(L-Ala-L-Ala) amino pyrrolidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro -7-{4'-(di-n-butylamino) piperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro -7-{4'-(t-butoxycarbonyl-L-Ala-L-Ala)aminopiperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro -7-(4'- propionoxy piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro -7-(4'-hydroxy-3',3'-dimethyl-piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6,8-difluoro-1, 4-dihydro -7-{4'-(1-pyrrolidinyl) piperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6,8-difluoro-1,4-dihydro-7-{4'-[(piperidin-4-yl) aminomethyl]-piperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro -7-{(1,2',2', 6',6'-pentamethyl piperidin-4-yl)methylamino}-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6,8-difluoro-1, 4-dihydro -7-(3',5'-dimethyl morpholin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro -7-(4'-cyclopropyl piperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro -7-(3', 5'-dimethyl-4-pivaloyl piperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

Ethyl 6,8-Difluoro-7-(4-hydroxypiperidin-1-yl)-1-(1-phenylthio-3(S)-but-3-yl)-1,4-dihydro-4-oxo-quinoline-3-carboxylate;

1- (2'-Trifluoromethylphenyl) -6-fluoro-1, 4-dihydro- -7-(3', 3', 4'-trimethyl piperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1- (2'-trifluoromethylphenyl)-6,8-difluoro-1, 4-dihydro -7-(morpholin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1- (2'-trifluoromethylphenyl) -6, 8-difluoro-1, 4-dihydro -7-(3',5'-dimethylmorpholin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1- (2'-trifluoromethylphenyl) -6, 8-difluoro-1, 4-dihydro -7-(3',5'-dimethyl piperazinyl-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1- (4'-trifluoromethylphenyl) -6, 8-difluoro-1, 4-dihydro -7-(3'-aminopyrrolidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1- (4'-Fluorophenyl) -6-fluoro-1,4-dihydro -7-{4'-ethylamino)piperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

1- (2',4'-Difluorophenyl) -6-fluoro-1, 4-dihydro-7-(3', 5'-dimethyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1- (2',4'-difluorophenyl) -6, 8-difluoro-1, 4-dihydro -7-(3'-hydroxy-5'-methylpyrrolidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1- (2',4'-difluorophenyl) -6, 8-difluoro-1, 4-dihydro -7-(3',3'-dimethyl piperazinyl-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro -7-{(3'-aminoethoxycarbonyl)pyrrolidin-3-yl}-4-oxo-naphthyridine-3-carboxylic acid and its salts

1-Cyclopropyl-6-fluoro-1,4-dihydro-7-(pyrrolidin-3-yl-amino)-4-oxo-naphthyridine-3-carboxylic acid and its salts;

1- (2',4'-Difluorophenyl) -6-fluoro-1, 4-dihydro -7-(piperidin-4-yl-amino)-4-oxo-naphthyridine-3-carboxylic acid and its salts;

Ethyl-1- (2',4'-difluorophenyl) -6-fluoro-1, 4-dihydro -7-{[1 α ,5 α ,6 α]-3-N-benzyl-3-azabicyclo[3.1.0]hex-6-yl-amino}-4-oxo-naphthyridine-3-carboxylate and its salts;

1-(2,4-difluorophenyl) -6-fluoro-7-(1-phenyl-4,5,6,7-tetrahydropyrazolo [4,3-c]pyridin-1-yl-1, 4-dihydro-4-oxo-1, 8-naphthyridine- 3-carboxylic acid and is salts;

(S)-(-)-9-Fluoro-6,7-dihydro-8-(4'-carboxamidopiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts;

(R)-(+)-9-Fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid L-arginine salt;

(S)-(-)-9-Fluoro-6,7-dihydro-8-(4'-hydroxy-3',3'-dimethylpiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts;

(S)-(-)-N-methylpiperidin-1-yl-9-fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylate;

(S)-(-)-Morpholinoethyl-9-fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylate and its salts;

Ethoxycarbonylmethyl (R)-(+)-9-fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylate;

N-1-{7-(1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid)}-N-3-amino-{7-(1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid)}-pyrrolidine;

N-1-{7-(1-cyclopropyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid)}-N-3-amino-{7-(1-cyclopropyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid)}-pyrrolidine;

N-1-{7-(1-cyclopropyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid)}-N-3-amino-{7-(1-cyclopropyl)-6,8-difluoro-5-amino-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid)}-pyrrolidine;

N-1-{7-(1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid)}-N-4-{7-(1-cyclopropyl-6,8-difluoro-5-amino-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid)}-piperazine;

N-1-{7-(1-cyclopropyl-6-fluoro-5-methyl-1,4-dihydro-4-oxo-quinolone-3-carboxylic acid)}-N-3-amino-{7-(1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid)}-pyrrolidine;

N-1-{7-(1-cyclopropyl-6-fluoro-5-methyl-1,4-dihydro-4-oxo-quinolone-3-carboxylic acid)}-N-4-amino-{7-(1-cyclopropyl-6,8-difluoro-5-amino-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid)}-piperidine;

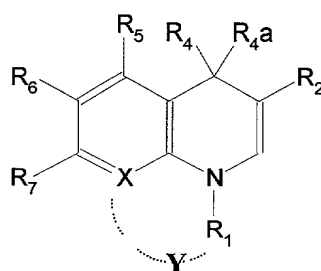
N-1-{7-(1-cyclopropyl-6-fluoro-5-methyl-1,4-dihydro-4-oxo-quinolone-3-carboxylic acid)}-N-3-amino-{7-(1-cyclopropyl-6,8-difluoro-5-amino-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid)}-pyrrolidine;

N-1-{7-(1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid)}-N-4-{7-(1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid)}-piperazine;

N-3-azabicyclo{7-(1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid)}-[1 α ,5 α ,6 α]-N-6-amino-{7-(1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid)}-[3.1.0] hexane; or

N-1-{7-(1-cyclopropyl-6,8-difluoro-5-amino-1,4-dihydro-4-oxo-quinolone-3-carboxylic acid)}-N-4-amino-{ethyl 2,3,6-trifluorophenyl-4-carboxylate}-piperidine.

39. An efflux pump inhibitor of the MexAB-OprM, MexCD-OprJ, MexEF-OprM, MexXY-OprM, AcrAB-TolC, AcrEF, MarA, SoxS and/or Tet pump/s, wherein said efflux pump inhibitor has the Structure 1 below



Structure 1

wherein,

R₁ = H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, or optionally substituted aryl, aralkyl, arylaminoalkyl, aryloxyalkyl, arylS(O)_talkyl, where t=0,1 or 2, or when X is C and the nitrogen atom to which R₁ is linked forms an optionally substituted 4-, 5-, 6- or 7-membered ring with X of the adjacent ring, the ring optionally containing one or more hetero atoms selected from nitrogen, oxygen or sulfur atoms said

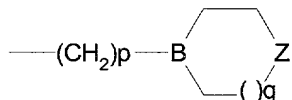
heteroatom(s) represented by Y, preferably R_1 is $-\text{CH}_2\text{CH}_2-$, $\text{CH}_2\text{Y}-$, $\text{CH}_2\text{CH}_2\text{CH}_2-$, $\text{CH}_2\text{CH}_2\text{Y}-$, $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2-$ and $\text{CH}_2\text{CH}_2\text{CH}_2\text{Y}-$ where Y represents NH, O, or S. If the ring is substituted, the substituent is C_{1-6} alkyl group;

$R_2 = \text{H, CHO, COOR}_3, \text{ or CONHR}_{13},$

where $R_{13} = \text{H}$ or the NHR_{13} of CONHR_{13} is the residue of one of the 20 naturally occurring amino acids: alanine, arginine, asparagines, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine or the optically active isomers thereof or the racemic mixtures thereof, or combinations of these amino acids to give dipeptidyl, tripeptidyl or polypeptidyl residues;

$R_3 = \text{H, C}_{1-6} \text{ alkyl, C}_{3-6} \text{ cycloalkyl, aryl, aralkyl, arylaminoalkyl, aryloxyalkyl, arylS(O)}_t\text{alkyl, where } t=0,1 \text{ or } 2,$
 $(\text{CH}_2)_n\text{CH(R}_{14})\text{OC(=O)R}_{15}, (\text{CH}_2)_n\text{CH(R}_{14})\text{C(=O)OR}_{15}$ wherein $n = 0-6$, $R_{14} = \text{H}$ or CH_3 ; and $R_{15} = \text{C}_2\text{H}_5$ or $\text{C(CH}_3)_3$;

or R_3 is



wherein $\text{B}=\text{CH}$ or N , and when $\text{B}=\text{CH}$, $\text{Z}=\text{NH}$ or NCH_3 , and when $\text{B}=\text{N}$, $\text{Z}=\text{CH}$, O , NH , S or NCH_3 ; $p=0-2$; $q=0-2$,

$R_4 = \text{H}$, $R_{4a} = \text{H}$, or R_4 and R_{4a} taken together are oxo ($=\text{O}$), or thio ($=\text{S}$);

$R_5 = \text{H}$, C_{1-5} alkyl, amino, alkylamino, or acylamino;

$R_6 = \text{H}$, C_{1-6} alkyl, halo, amino, or hydroxy;

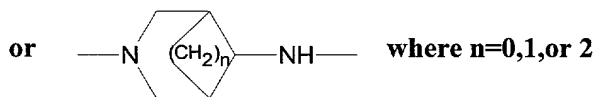
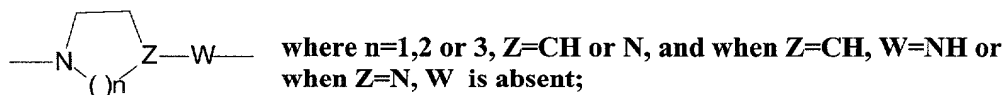
$R_7 = \text{OH}$, halo or

NR_9 , R_{10} wherein R_9 and R_{10} are the same or different and represent H , C_{1-6} alkyl or $(\text{CH}_2)_n\text{OA}$,

or R_9 is H and R_{10} is a 4-membered, 5-membered, 6-membered, or 7-membered carbocyclic, mono or bicyclic ring or mono or bicyclic heterocyclic ring linked to the nitrogen of NR_9R_{10} through an atom of the heterocycle other than the heterocyclic atom or R_9 and R_{10} taken together with the nitrogen atom to which they are attached form part of a heterocycle which heterocycle is monocyclic, bicyclic, and said carbocycle and heterocycle is optionally substituted;

or $R_7 = \text{NHOA}$, NHCOOR_{11} , or $\text{NH(CH}_2)_n\text{NR}_9\text{R}_{10}$;

or $R_7 =$



wherein the R_7 moiety is linked either to 2 core molecules of the Formula I to form a bis compound or the R_7 moiety has one of its link bonds linked to the core formula of Formula I and the second of its link bonds is linked to an optionally substituted phenyl carboxylic acid or ester moiety thereof,

$\text{A} = \text{H}$, C_{1-6} alkyl, glycosyl, aralkyl, C_{1-6} alkanoyl or aminoalkanoyl wherein the aminoalkanoyl group may be an aminoacid residue derived from one of the one of the 20 naturally occurring amino acids or the optically active isomers thereof, or the racemic mixtures thereof wherein the amino residue is derived from alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine; or.

A is C₆H₁₁O₆, SO₃H, or PO₃H₂,

R₁₁ = H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, or heterocyclic group,

X = CH, C-F, C-Cl, C-CH₃, C-CF₃, C-OCH₃, C-OCHF₂, C-OCF₃, N or when X is equal to C it forms together with the nitrogen atom of the adjacent ring an optionally substituted 5-membered ring, 6-membered ring, 7-membered ring, containing carbon atoms and optionally Y atoms representing one or more nitrogen, oxygen or sulfur atoms; if the ring is substituted, the substituent is C₁₋₆ alkyl group;

and their pharmaceutically acceptable salts, hydrates, polymorphs and pseudopolymorphs.

40. The efflux pump inhibitor according to claim 39 selected from:

1-Cyclopropyl-6-fluoro-1, 4-dihydro-5-methyl- 7-(4'-methoxypiperidin -1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

7-Bromo-1-cyclopropyl-6-fluoro-5-methyl-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1, 4-dihydro -7-(4'-amino-3'-methylpiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-amino-3'-methyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro -7-{3,3-dimethyl-4'-ethylamino piperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-amino-3'-3'-dimethyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-{4'-(dimethylamino)piperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-hydroxy-4'-methylpiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(3',3'-dimethyl-4'-hydroxypiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6,8-difluoro-5-methyl-1,4-dihydro-7-(3'-aminomethyl-4'-hydroxypiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6,8-difluoro-1,4-dihydro-7-(3'-aminomethyl-4'-hydroxypiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Ethyl-6,8-difluoro-1,4-dihydro-7-(3'-5'-dimethylpiperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1,4-dihydro-7-(4'-ethyl-3'-methylpiperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1,4-dihydro-7-(3'-5'-dimethyl-4'-ethylpiperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Ethyl-6, 8-difluoro-1, 4-dihydro -7- $\{1\alpha,5\alpha,6\alpha\}$ -6'-amino-3'-azabicyclo [3.1.0] hex-3'-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-(2',4'-difluorophenyl)-6,8-difluoro-1,4-dihydro-7-(3'-aminopyrrolidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6,8-difluoro-1,4-dihydro-7- $\{3'$ -aminoethoxycarbonyl pyrrolidin-3-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1,4-dihydro-7-(pyrrolidin-3'-ylamino)-4-oxo-naphthyridine-3-carboxylic acid and its salts;

1-(2',4'-Difluorophenyl)-6-fluoro-1,4-dihydro-7-(piperidin-4'-ylamino)-4-oxo-naphthyridine-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro -7-(4'-amino-3'-ethylpiperidin-1-yl)-4-oxo-naphthyridine-3-carboxylic acid and its salts;

(S)-(-)-9-Fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid 0.2 hydrate;

(S)-(-)-9-Fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid . choline salt;

(S)-(-)-9-Fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid. 1-Hydroxyethylpyrrolidine salt.

(S)-(-)-9-Fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid. Diethanolamine salt;

(S)-(-)-9-Fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylate. L-histidine salt;

(RS)-(\pm)-9-Fluoro-6,7-dihydro-8-{4'-(D-phenylalanyloxy) piperidin-1-yl}-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid hydrochloride;

(RS)-(\pm)-9-Fluoro-6,7-dihydro-8-{4'-(L- α -aspartylloxy) piperidin-1-yl}-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid hydrochloride;

(\pm)-9-Fluoro-6,7-dihydro-8-{4'-(L-leucylloxy)piperidin-1-yl}-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid dihydrochloride;

(-)-9-Fluoro-6,7-dihydro-8-{4'-(D-leucylloxy)piperidin-1-yl}-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid hydrochloride;

(S)-(-)-9-Fluoro-6,7-dihydro-8-{4'-(L-alanyloxy)piperidin-1-yl}-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid hydrochloride;

(S)-(-)-Morpholinoethyl-9-fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylate and its salts;

(R)-(+)-8,9-difluoro-6,7-dihydro-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2- [S-phenylalanyl-S-lysine methyl ester]carboxamide;

(RS)-(±)-9-Fluoro-6,7-dihydro-8-(trans-4'-hydroxy-3'-methylpiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts;

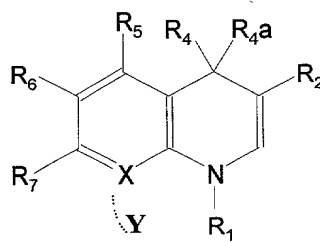
(RS)-(±)-9-Fluoro-6,7-dihydro-8-(cis-4'-hydroxy-3'-methylpiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts;

(S)-(-)-9-Fluoro-6,7-dihydro-8-(trans-4'-hydroxy-3'-methylpiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts;

7H-Pyrido[1,2,3-de]-1,4-benzoxazine-9-fluoro-2,3-dihydro-3-methyl-10-(4'-hydroxy-3'-ethylpiperidin-1'-yl)-7-oxo-6-carboxylic acid and its salts;

10-Fluoro-11-[(1α,5α,6α)-6-amino-3-azabicyclo[3.1.0]hex-3-yl]-3,4-dihydro-4(S)-methyl-8-oxo-2H,8H-pyrido[1,2,3-ef]-1,5-benzoxazepine-7-carboxylic acid. Hydrochloride;

41. A pharmaceutical composition effective for treatment of an infection of an animal by a microbe, comprising an efflux pump inhibitor and a pharmaceutically acceptable carrier, wherein said efflux pump inhibitor has the chemical structure of structure 1 below:



Structure 1

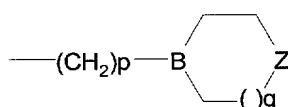
wherein,

$R_1 =$ H, C_{1-6} alkyl, C_{3-6} cycloalkyl, or optionally substituted aryl, aralkyl, arylaminoalkyl, aryloxyalkyl, arylS(O)_talkyl, where $t=0,1$ or 2 , or when X is C and the nitrogen atom to which R_1 is linked forms an optionally substituted 4-, 5-, 6- or 7-membered ring with X of the adjacent ring, the ring optionally containing one or more hetero atoms selected from nitrogen, oxygen or sulfur atoms said heteroatom(s) represented by Y, preferably R_1 is $-CH_2CH_2-$, CH_2Y- , $CH_2CH_2CH_2-$, CH_2CH_2Y- , $CH_2CH_2CH_2CH_2-$ and $CH_2CH_2CH_2Y-$ where Y represents NH, O, or S. If the ring is substituted, the substituent is C_{1-6} alkyl group;

$R_2 =$ H, CHO, COOR₃, or CONHR₁₃, where $R_{13} =$ H or the NHR₁₃ of CONHR₁₃ is the residue of one of the 20 naturally occurring amino acids: alanine, arginine, asparagines, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine or the optically active isomers thereof or the racemic mixtures thereof, or combinations of these amino acids to give dipeptidyl, tripeptidyl or polypeptidyl residues;

$R_3 =$ H, C_{1-6} alkyl, C_{3-6} cycloalkyl, aryl, aralkyl, arylaminoalkyl, aryloxyalkyl, arylS(O)_talkyl, where $t=0,1$ or 2 , $(CH_2)_nCH(R_{14})OC(=O)R_{15}$, $(CH_2)_nCH(R_{14})C(=O)OR_{15}$ wherein $n = 0-6$, $R_{14} =$ H or CH_3 ; and $R_{15} = C_2H_5$ or $C(CH_3)_3$;

or R_3 is



wherein B=CH or N, and when B=CH, Z=NH or NCH₃, and when B=N, Z=CH, O, NH, S or NCH₃; p=0-2; q=0-2,

R₄ = H, R_{4a} = H, or R₄ and R_{4a} taken together are oxo (=O), or thio (=S);

R₅ = H, C₁₋₅ alkyl, amino, alkylamino, or acylamino;

R₆ = H, C₁₋₆ alkyl, halo, amino, or hydroxy;

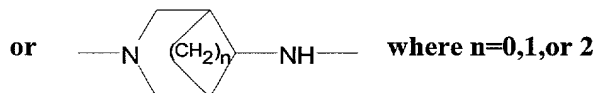
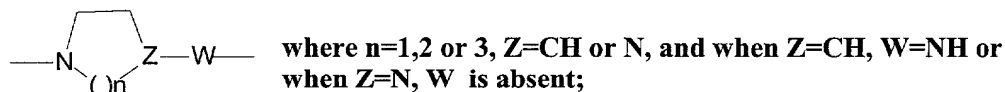
R₇ = OH, halo or

NR₉R₁₀ wherein R₉ and R₁₀ are the same or different and represent H, C₁₋₆ alkyl or (CH₂)_nOA,

or R₉ is H and R₁₀ is a 4-membered, 5-membered, 6-membered, or 7-membered carbocyclic, mono or bicyclic ring or mono or bicyclic heterocyclic ring linked to the nitrogen of NR₉R₁₀ through an atom of the heterocycle other than the heterocyclic atom or R₉ and R₁₀ taken together with the nitrogen atom to which they are attached form part of a heterocycle which heterocycle is monocyclic, bicyclic, and said carbocycle and heterocycle is optionally substituted;

or R₇ = NHOA, NHCOOR₁₁, or NH(CH₂)_nNR₉R₁₀;

or R₇ =



wherein the R₇ moiety is linked either to 2 core molecules of the Formula I to form a bis compound or the R₇ moiety has one of its link bonds linked to the core formula of Formula I and the second of its link bonds is linked to an optionally substituted phenyl carboxylic acid or ester moiety thereof,

A = H, C₁₋₆ alkyl, glycosyl, aralkyl, C₁₋₆ alkanoyl or aminoalkanoyl wherein the aminoalkanoyl group may be an aminoacid residue derived from one of the one of the 20 naturally occurring amino acids or the optically active isomers thereof, or the racemic mixtures thereof wherein the amino residue is derived from alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine; or.

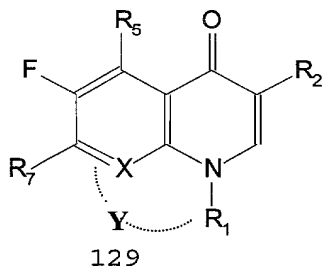
A is C₆H₁₁O₆, SO₃H, or PO₃H₂,

R₁₁ = H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, or heterocyclic group,

X = CH, C-F, C-Cl, C-CH₃, C-CF₃, C-OCH₃, C-OCHF₂, C-OCF₃, N or when X is equal to C it forms together with the nitrogen atom of the adjacent ring an optionally substituted 5-membered ring, 6-membered ring, 7-membered ring, containing carbon atoms and optionally Y atoms representing one or more nitrogen, oxygen or sulfur atoms; if the ring is substituted, the substituent is C₁₋₆ alkyl group;

and their pharmaceutically acceptable salts, hydrates, polymorphs and pseudopolymorphs;

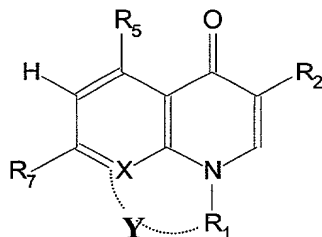
42. A pharmaceutical composition according to claim 41 wherein said efflux pump inhibitor has structure 2



Structure 2

wherein R1, R2,, R5, R7, X and Y are as defined in claim 1.

43. A pharmaceutical composition according to claim 41, wherein said efflux pump inhibitor has the chemical structure 3 below



Structure 3

wherein R1, R2, R5, R7, X and Y are as defined in claim 1.

44. The pharmaceutical composition of claim 41, wherein said microbe is a bacterium.

45. The pharmaceutical composition of claim 41 further comprising an antimicrobial agent.

46. The pharmaceutical composition of claim 45, wherein said microbe is a bacterium.

47. The pharmaceutical composition of claims 41 and 46, wherein said antimicrobial agent is an antibacterial agent.

48. The pharmaceutical composition of claims 41 further comprising a macrolide.

49. The pharmaceutical composition of claim 48, wherein the said macrolide/ketolide is selected from the group consisting of azithromycin, telithromycin, clarithromycin, erythromycin, rokitamycin, roxithromycin, spiramyci and josamycin.

50. The pharmaceutical composition of claims 41 and 49, wherein the said efflux pump inhibitor is

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-amino-3'-methyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-{4'-(methylamino)-3',3'-dimethylpiperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

i-Propyl 1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-amino-3',3'-dimethyl-piperidin-1-yl)-4-oxo-quinoline-3-carboxylate and its salts;

n-Butyl 1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-amino-3',3'-dimethyl-piperidin-1-yl)-4-oxo-quinoline-3-carboxylate and its salts;

Ethoxycarbonylmethyl 1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-amino-3',3'-dimethylpiperidin-1-yl)-4-oxo-quinoline-3-carboxylate and its salts;

Benzyl 1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-{4'-(t-butoxycarbonyl amino)-3',3'-dimethylpiperidin-1-yl}-4-oxo-quinoline-3-carboxylate and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-{4'-N-(t-butoxycarbonyl-L-alanyl) amino-3',3'-dimethylpiperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid hydrochloride;

1-Cyclopropyl-6-fluoro-8-methoxy-1, 4-dihydro -7-(4'-L-alanyl-amino-3',3'-dimethylpiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid hydrochloride;

1-Cyclopropyl-6-fluoro-8-methoxy-1, 4-dihydro -7-(3',3'-dimethyl-4'-(t-butoxy-carbonylvalinyl-amino)piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro -7-(3',3'-dimethyl-4'-(L)-valyl-aminopiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid hydrochloride;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-{4'-(L)-aspartyl-amino-3',3'-dimethylpiperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid hydrochloride;

1-Ethyl-6,8-difluoro-1,4-dihydro-7-(4'-ethylaminopiperidin-1'-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6,8-difluoro-1,4-dihydro-7-(4'-amino-3'-methyl piperidin -1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6,8-difluoro-1,4-dihydro-7-(quinuclidinyl-3-yl-amino)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro-7- {(1 α ,5 α ,6 α)-6-amino-N-benzyl-3-azabicyclo [3.1.0] hex-6-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

1-(3'-Fluorophenyl)-6-fluoro -1, 4-dihydro -7-(4'-methylpiperazin-1'-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-(2,4-Difluorophenyl) -6-fluoro-1, 4-dihydro-7- (4'-ethylaminopiperidin-1'-yl)- 4-oxo-quinoline-3-carboxylic acid and its salts;

1-(2',4'-Difluorophenyl)-6-fluoro-5-methyl-1, 4-dihydro -7-(4'-aminopiperidin-1'-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-(2',4'-Difluorophenyl)-6-fluoro-5-methyl-1,4-dihydro-7-(4'-methylamino piperidin-1'-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1,4-dihydro-7-(3'-aminopyrrolidin-1'-yl)-4-oxo-1,8-naphthyridine-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1,4-dihydro-7- {(1 α ,5 α ,6 α)-6-amino--N-benzyl-3-azabicyclo [3.1.0] hex-6-yl}-4-oxo-1,8-naphthyridine-3-carboxylic acid and its salts;

1-(2,4-Difluorophenyl) -6-fluoro-1, 4-dihydro-7-(3'-aminopyrrolidin-1'-yl)- 4-oxo-1,8-naphthyridine-3-carboxylic acid and its salts;

1-(2,4-Difluorophenyl) -6-fluoro-1, 4-dihydro-7- {(1 α ,5 α ,6 α)-6-amino-N-benzyl-3-azabicyclo [3.1.0]hex-6-yl}- 4-oxo-1,8-naphthyridine-3-carboxylic acid and its salts;

1-(2,4-Difluorophenyl)-6-fluoro-1,4-dihydro-7-(3',3'-dimethyl-4'-hydroxy piperidin-1'-yl)-4-oxo-1,8-naphthyridine-3-carboxylic acid and its salts;

(RS)-(\pm)-9-Fluoro-6, 7-dihydro-8-{4'-(L- α -aspartyl-oxy)piperidin-1-yl}-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid hydrochloride;

7H-Pyrido[1,2,3-de]-1,4-benzoxazine-9-fluoro-2,3-dihydro-3-methyl-10-(3'-ethyl 4'-

hydroxypiperidin-1'-yl)-7-oxo-6-carboxylic acid and its salts;

7H-Pyrido[1,2,3-de]-1,4-benzoxazine-9-fluoro-2,3-dihydro-3-methyl-10-(3'-amino methyl-4'-

hydroxypiperidin-1'-yl)-7-oxo-6-carboxylic acid and its salt;

5 1-Cyclopropyl-6,8-difluoro-5-methyl-1,4-dihydro-7-(3',3'-dimethyl-4'-ethylamino piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salt;

1-cyclopropyl-6,7,8-trifluoro-5-methyl-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid;

(S)-(-)-9-Fluoro-6,7-dihydro-8-(3',3'-dimethyl-4'-ethylaminopiperidin-1-yl)-5-methyl-1-oxo-1H, 5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts;

10 1-Cyclopropyl-6-fluoro-1,4-dihydro-7-(3'-aminomethyl-4'-hydroxypiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1,4-dihydro-7-(4'-dimethylamino-3'-methylpiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-{4'-cyclopropyl aminopiperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-(t-butoxycarbonyl (L)-Ala-Ala)amino-3',3'-dimethyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid hydrochloride;

5-Amino-1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-{4'-ethylamino-3',5'-dimethylpiperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

20 Ethyl 1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-7-(4-amino-3-ethylpiperidin-1-yl)-4-oxo-1,8-naphthyridine-3-carboxylate;

1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-7-(4-amino-3,5-dimethylpiperidin-1-yl)-4-oxo-1,8-naphthyridine-3-carboxylic acid and its salts;

25 Ethyl 1-(2,4-difluorophenyl)-6-fluoro-5-methyl-1,4-dihydro-7-(4-amino-3,3-dimethylpiperidin-1-yl)-4-oxo-1,8-naphthyridine-3-carboxylate;

(S)-(-)-9-fluoro-6,7-dihydro-8-(4'-hydroxy-3'-fluoropiperidin-1-yl)-5-methyl-1-oxo-1H, 5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts;

10-Fluoro-11-(4-aminopiperidin-1-yl)-3,4-dihydro-4(S)-methyl-8-oxo-2H, 8H-pyrido[1,2,3-ef]-1,5-benzoxazepin-7-carboxylic acid and its salt;

30 (RS)-(±)-6,7-dihydro-8-(trans-4'-hydroxy-3'-methylpiperidin-1-yl)-5-methyl-1-oxo-1H, 5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts;

(RS)-(±)-6,7-dihydro-8-(cis-4'-hydroxy-3'-methylpiperidin-1-yl)-5-methyl-1-oxo-1H, 5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts; or

(RS)-(±)-6,7-dihydro-8-(4'-hydroxy-3',3'-dimethylpiperidin-1-yl)-5-methyl-1-oxo-1H, 5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts.

51. The pharmaceutical composition of Claim 41 further comprising a fluoroquinolone.

52. The pharmaceutical composition of claim 51, wherein the said fluoroquinolone is selected from the group consisting of ciprofloxacin, norfloxacin, levofloxacin, clinafloxacin, sitafloxacin, gatifloxacin, moxifloxacin, trovafloxacin, gemifloxacin and nadifloxacin.

53. The pharmaceutical composition of claims 41 and 52, wherein the said efflux pump inhibitor is:

1-Ethyl-6-fluoro-1, 4-dihydro -7-(1', 2',3',4'-tetrahydroisoquinolin-2-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Ethyl-6, 8-fluoro-1, 4-dihydro -7-(4'-acetoxypiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Ethyl-6, 8-fluoro-1, 4-dihydro -7-(4'-{2'-(2'-oxazolidin-1-yl) ethyl} piperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Ethyl-6, 8-difluoro-1, 4-dihydro -7-{(1 α ,5 α ,6 α)-6-amino-3-azabicyclo [3.1.0]-hex-3-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-ethyl-6, 8-difluoro-1, 4-dihydro -7-(3'-amino-5'-methyl pyrrolidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-ethyl-6, 8-difluoro-1, 4-dihydro -7-(4'-aminopiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-ethyl-6, 8-difluoro-1, 4-dihydro -7-{4'-(acetamido) piperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-ethyl-6, 8-difluoro-1, 4-dihydro -7-{(1 α ,5 α ,6 α)-6'-(t-butoxycarbonyl amino)-3-azabicyclo [3.1.0]-hex-3-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro-7-(3'-acetamido-5'-methylpyrrolidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro-7-(3'-amino-5'-methylpyrrolidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1,4-dihydro--7-(4'-acetoxypiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1,4-dihydro -7-{4'-(dimethylamino) piperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1,4-dihydro-7-(3',5'-dimethylpiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro -7-(4'-hydroxy-3',5'-dimethylpiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro- -7-(3', 4', 5'-trimethyl piperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro- 7-(3', 5'-dimethyl-4'-ethyl piperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5 1-Cyclopropyl-6-fluoro-1, 4-dihydro-5-methyl- 7-(4'-ethoxypiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro-5-methyl- 7-(3', 3'-dimethylpiperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

10 1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-{4'-(dimethylamino)-3'-methyl piperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-hydroxy-3'-isobutyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-hydroxy-3',3'-dimethyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5 1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-hydroxy-3',5'-dimethyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(3'-methylpiperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5 5-Amino-1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(cis-4'-amino-3',5'-dimethylpiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6,8-difluoro-5-methyl-1,4-dihydro-7-(4'-hydroxy-3'-aminomethyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6,8-difluoro-1,4-dihydro-7-(5'-amino-2'-methyl-pyrrolidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

25 5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro -7-{3'-(L-Ala-L-Ala) amino pyrrolidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro -7-{4'-(di-n-butylamino) piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

30 5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro -7-{4'-(t-butoxycarbonyl-L-Ala-L-Ala)aminopiperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro -7-(4'- propionoxy piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro -7-(4'-hydroxy-3',3'-dimethyl-piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

35 5-Amino-1-cyclopropyl-6,8-difluoro-1, 4-dihydro -7-{4'-(1-pyrrolidinyl) piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6,8-difluoro-1,4-dihydro-7-{4'-[(piperidin-4-yl) aminomethyl]-piperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro -7-[(1,2',2', 6',6'-pentamethyl piperidin-4-yl)methylamino]-4-oxo-quinoline-3-carboxylic acid and its salts;

5 5-Amino-1-cyclopropyl-6,8-difluoro-1, 4-dihydro -7-(3',5'-dimethyl morpholin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro -7-(4'-cyclopropyl piperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro -7-(3', 5'-dimethyl-4-pivaloyl piperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

10 Ethyl 6,8-Difluoro-7-(4-hydroxypiperidin-1-yl)-1-(1-phenylthio-3(S)-but-3-yl)-1,4-dihydro-4-oxo-quinoline-3-carboxylate;

1- (2'-Trifluoromethylphenyl) -6-fluoro-1, 4-dihydro- -7-(3', 3', 4'-trimethyl piperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5 5-Amino-1- (2'-trifluoromethylphenyl)-6,8-difluoro-1, 4-dihydro -7-(morpholin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1- (2'-trifluoromethylphenyl) -6, 8-difluoro-1, 4-dihydro -7-(3',5'-dimethylmorpholin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1- (2'-trifluoromethylphenyl) -6, 8-difluoro-1, 4-dihydro -7-(3',5'-dimethyl piperazinyl-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

20 5-Amino-1- (4'-trifluoromethylphenyl) -6, 8-difluoro-1, 4-dihydro -7-(3'-aminopyrrolidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1- (4'-Fluorophenyl) -6-fluoro-1,4-dihydro -7-{4'-ethylamino)piperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

25 1- (2',4'-Difluorophenyl) -6-fluoro-1, 4-dihydro-7-(3', 5'-dimethyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1- (2',4'-difluorophenyl) -6, 8-difluoro-1, 4-dihydro -7-(3'-hydroxy-5'-methylpyrrolidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1- (2',4'-difluorophenyl) -6, 8-difluoro-1, 4-dihydro -7-(3',3'-dimethyl piperazinyl-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

30 1-Cyclopropyl-6-fluoro-1, 4-dihydro -7-[(3'-aminoethoxycarbonyl)pyrrolidin-3-yl]-4-oxo-naphthyridine-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1,4-dihydro-7-(pyrrolidin-3-yl-amino)-4-oxo-naphthyridine-3-carboxylic acid and its salts;

35 1- (2',4'-Difluorophenyl) -6-fluoro-1, 4-dihydro -7-(piperidin-4-yl-amino)-4-oxo-naphthyridine-3-carboxylic acid and its salts;

Ethyl-1- (2',4'-difluorophenyl) -6-fluoro-1, 4-dihydro -7-{[1 α ,5 α ,6 α]-3-N-benzyl-3-azabicyclo[3.1.0]hex-6-yl-amino}-4-oxo-naphthyridine-3-carboxylate and its salts;
 1-(2,4-difluorophenyl) -6-fluoro-7-(1-phenyl-4,5,6,7-tetrahydropyrazolo [4,3-c]pyridin-1-yl-1, 4-dihydro-4-oxo-1, 8-naphthyridine- 3-carboxylic acid and its salts;
 5 (S)-(-)-9-Fluoro-6,7-dihydro-8-(4'-carboxamidopiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts;
 (R)-(+)-9-Fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid L-arginine salt;
 (S)-(-)-9-Fluoro-6,7-dihydro-8-(4'-hydroxy-3',3'-dimethylpiperidin-1-yl)-5-methyl-1-oxo-1H,5H-
 10 benzo[i,j]quinolizine-2-carboxylic acid and its salts;
 (S)-(-)-N-methylpiperidin-1-yl-9-fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylate;
 (S)-(-)-Morpholinoethyl-9-fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylate and its salts;
 5 Ethoxycarbonylmethyl (R)-(+)- 9-fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylate;
 N-1-{7-(1-cyclopropyl-6-fluoro-1, 4-dihydro-4-oxo-quinoline-3-carboxylic acid)}-N-3-amino-{7-(1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid)}-pyrrolidine;
 20 N-1-{7-(1-cyclopropyl) -6-fluoro-1, 4-dihydro-4-oxo-1, 8-naphthyridine- 3-carboxylic acid)}-N-3-amino-{7-(1-cyclopropyl) -6-fluoro-1, 4-dihydro-4-oxo-1, 8-naphthyridine- 3-carboxylic acid)}-pyrrolidine;
 N-1-{7-(1-cyclopropyl) -6-fluoro-1, 4-dihydro-4-oxo-1, 8-naphthyridine- 3-carboxylic acid)}-N-3-amino-{7-(1-cyclopropyl -6,8-difluoro-5-amino-1, 4-dihydro-4-oxo-quinoline-3-carboxylic acid)}-pyrrolidine;
 25 N-1-{7-(1-cyclopropyl-6-fluoro-1, 4-dihydro-4-oxo-1, 8-naphthyridine- 3-carboxylic acid)}-N-4-{7-(1-cyclopropyl-6,8-difluoro-5-amino-1, 4-dihydro-4-oxo-quinoline-3-carboxylic acid)}-piperazine;
 N-1-{7-(1-cyclopropyl-6-fluoro-5-methyl-1,4-dihydro-4-oxo-quinolone-3-carboxylic acid)}-N-3-amino-{7-(1-(2,4-difluorophenyl) -6-fluoro- 1, 4-dihydro-4-oxo-1, 8-naphthyridine-3-carboxylic acid)}-pyrrolidine;
 30 N-1- {7-(1-cyclopropyl-6-fluoro-5-methyl-1, 4-dihydro-4-oxo-quinolone-3-carboxylic acid)}-N-4-amino {7-(1-cyclopropyl-6,8-difluoro-5-amino-1, 4-dihydro-4-oxo-quinoline-3-carboxylic acid)}-piperidine;
 N-1- {7-(1-cyclopropyl-6-fluoro-5-methyl-1, 4-dihydro-4-oxo-quinolone-3-carboxylic acid)}-N-3-
 35 amino{7-(1-cyclopropyl-6,8-difluoro-5-amino-1, 4-dihydro-4-oxo-quinoline-3-carboxylic acid)}-pyrrolidine;

N-1- {7-(1-(2,4-difluorophenyl) -6-fluoro-1, 4-dihydro-4-oxo-1, 8-naphthyridine- 3-carboxylic acid))-N-4- {7-(1-cyclopropyl-6-fluoro-1, 4-dihydro-4-oxo-quinoline-3-carboxylic acid))-piperazine;
 N-3-azabicyclo{7-(1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid))-[1 α ,5 α ,6 α]-N-6-amino-{7-1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid))-[3.1.0] hexane; or
 N-1- {7-(1-cyclopropyl-6,8-difluoro-5-amino-1, 4-dihydro-4-oxo-quinolone-3-carboxylic acid))-N-4-amino-{ethyl 2,3,6-trifluorophenyl-4-carboxylate))-piperidine.

54. The pharmaceutical composition of Claim 41 further comprising antimicrobial agents selected from the group of ciprofloxacin, levofloxacin, ofloxacin, gemifloxacin, nadifloxacin azithromycin, erythromycin, tetracycline, linezolid and novobiocin.

55. The pharmaceutical composition of claim 41 and 54, wherein the said efflux pump inhibitor is

1-Cyclopropyl-6-fluoro-1, 4-dihydro-5-methyl- 7-(4'-methoxypiperidin -1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

7-Bromo-1-cyclopropyl-6-fluoro-5-methyl-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1, 4-dihydro -7-(4'-amino-3'-methylpiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-amino-3'-methyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro -7-{3,3-dimethyl-4'-ethylamino piperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-amino-3'-3'-dimethyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-{4'-(dimethylamino)piperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-hydroxy-4'-methylpiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(3',3'-dimethyl-4'-hydroxypiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6,8-difluoro-5-methyl-1,4-dihydro-7-(3'-aminomethyl-4'-hydroxypiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6,8-difluoro-1,4-dihydro-7-(3'-aminomethyl-4'-hydroxypiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Ethyl-6,8-difluoro-1,4-dihydro-7-(3'-5'-dimethylpiperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5 1-Cyclopropyl-6-fluoro-1,4-dihydro-7-(4'-ethyl-3'-methylpiperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1,4-dihydro-7-(3'-5'-dimethyl-4'-ethylpiperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

10 1-Ethyl-6, 8-difluoro-1, 4-dihydro -7-((1 α ,5 α ,6 α)-6'-amino-3'-azabicyclo [3.1.0] hex-3'-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-(2',4'-difluorophenyl)-6,8-difluoro-1,4-dihydro-7-(3'-aminopyrrolidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6,8-difluoro-1,4-dihydro-7-((3'-aminoethoxycarbonyl pyrrolidin-3-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

15 1-Cyclopropyl-6-fluoro-1,4-dihydro-7-(pyrrolidin-3'-ylamino)-4-oxo-naphthyridine-3-carboxylic acid and its salts;

1-(2',4'-Difluorophenyl)-6-fluoro-1,4-dihydro-7-(piperidin-4'-ylamino)-4-oxo-naphthyridine-3-carboxylic acid and its salts;

20 1-Cyclopropyl-6-fluoro-1, 4-dihydro -7-(4'-amino-3'-ethylpiperidin-1-yl)-4-oxo-naphthyridine-3-carboxylic acid and its salts;

(S)-(-)-9-Fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid 0.2 hydrate;

(S)-(-)-9-Fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid . choline salt;

25 (S)-(-)-9-Fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid. 1-Hydroxyethylpyrrolidine salt;

(S)-(-)-9-Fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid. Diethanolamine salt;

30 (S)-(-)-9-Fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylate. L-histidine salt;

(RS)-(\pm)-9-Fluoro-6,7-dihydro-8-{4'-(D-phenylalanyloxy) piperidin-1-yl}-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid hydrochloride;

(RS)-(\pm)-9-Fluoro-6,7-dihydro-8-{4'-(L- α -aspartylloxy) piperidin-1-yl}-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid hydrochloride;

35 (RS)-(\pm)-9-Fluoro-6,7-dihydro-8-{4'-(L-leucylloxy)piperidin-1-yl}-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid dihydrochloride;

(S)-(-)-9-Fluoro-6,7-dihydro-8-{4'-(D-leucyloxy)piperidin-1-yl}-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid hydrochloride;

(S)-(-)-9-Fluoro-6,7-dihydro-8-{4'-(L-alanyloxy)piperidin-1-yl}-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid hydrochloride;

5 (S)-(-)-Morpholinoethyl-9-fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylate and its salts;

(R)-(+)-8,9-difluoro-6,7-dihydro-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2- [S-phenylalanyl-S-lysine methyl ester]carboxamide;

(RS)-(\pm)-9-Fluoro-6,7-dihydro-8-(trans-4'-hydroxy-3'-methylpiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts;

10 (RS)-(\pm)-9-Fluoro-6,7-dihydro-8-(cis-4'-hydroxy-3'-methylpiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts;

(S)-(-)-9-Fluoro-6,7-dihydro-8-(trans-4'-hydroxy-3'-methylpiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts;

5 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-9-fluoro-2,3-dihydro-3-methyl-10-(4'-hydroxy-3'-ethylpiperidin-1'-yl)-7-oxo-6-carboxylic acid and its salts; or

10-Fluoro-11-[(1 α ,5 α ,6 α)-6-amino-3-azabicyclo[3.1.0]hex-3-yl]-3,4-dihydro-4(S)-methyl-8-oxo-2H,8H-pyrido[1,2,3-ef]-1,5-benzoxazepine-7-carboxylic acid, hydrochloride.

20 56. The method according to any one of claims 1,4,8, or 11 wherein the efflux pump inhibitor is selected from:

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-amino-3'-methyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

25 5-Amino-1-cyclopropyl-6-fluoro-8-methoxy-1, 4-dihydro -7-{4'-(methylamino)-3',3'-dimethylpiperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

i-Propyl 1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro -7-(4'-amino-3',3'-dimethyl-piperidin-1-yl)-4-oxo-quinoline-3-carboxylate and its salts;

n-Butyl 1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro -7-(4'-amino-3',3'-dimethyl-piperidin-1-yl)-4-oxo-quinoline-3-carboxylate and its salts;

30 Ethoxycarbonylmethyl 1-cyclopropyl-6-fluoro-8-methoxy-1, 4-dihydro -7-(4'-amino-3',3'-dimethylpiperidin-1-yl)-4-oxo-quinoline-3-carboxylate and its salts;

Benzyl 1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro -7-{4'-(t-butoxycarbonyl amino)-3',3'-dimethylpiperidin-1-yl}-4-oxo-quinoline-3-carboxylate and its salts;

35 1-Cyclopropyl-6-fluoro-8-methoxy-1, 4-dihydro -7-{4'-N-(t-butoxycarbonyl-L-alanyl) amino-3',3'-dimethylpiperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid hydrochloride;

1-Cyclopropyl-6-fluoro-8-methoxy-1, 4-dihydro -7-(4'-L-alanyl-amino-3',3'-dimethylpiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid hydrochloride;

1-Cyclopropyl-6-fluoro-8-methoxy-1, 4-dihydro -7-(3',3'-dimethyl-4'-(t-butoxy-carbonylvalinyl-amino)piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5 1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro -7-(3',3'-dimethyl-4'-(L)-valyl-aminopiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid hydrochloride;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-{4'-(L)-aspartyl-amino-3',3'-dimethylpiperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid hydrochloride;

10 1-Ethyl-6,8-difluoro-1,4-dihydro-7-(4'-ethylaminopiperidin-1'-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6,8-difluoro-1,4-dihydro-7-(4'-amino-3'-methyl piperidin -1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6,8-difluoro-1,4-dihydro-7-(quinuclidinyl-3-yl-amino)-4-oxo-quinoline-3-carboxylic acid and its salts;

5 5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro-7- {(1 α ,5 α ,6 α)-6-amino-N-benzyl-3-azabicyclo [3.1.0] hex-6-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

1-(3'-Fluorophenyl)-6-fluoro -1, 4-dihydro -7-(4'-methylpiperazin-1'-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

20 1-(2,4-Difluorophenyl) -6-fluoro-1, 4-dihydro-7- (4'-ethylaminopiperidin-1'-yl)- 4-oxo-quinoline-3-carboxylic acid and its salts;

1-(2',4'-Difluorophenyl)-6-fluoro-5-methyl-1, 4-dihydro -7-(4'-aminopiperidin-1'-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-(2',4'-Difluorophenyl)-6-fluoro-5-methyl-1,4-dihydro-7-(4'-methylamino piperidin-1'-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

25 1-Cyclopropyl-6-fluoro-1,4-dihydro-7-(3'-aminopyrrolidin-1'-yl)-4-oxo-1,8-naphthyridine-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1,4-dihydro-7-{(1 α ,5 α ,6 α)-6-amino-N-benzyl-3-azabicyclo [3.1.0] hex-6-yl}-4-oxo-1,8-naphthyridine-3-carboxylic acid and its salts;

30 1-(2,4-Difluorophenyl) -6-fluoro-1, 4-dihydro-7-(3'-aminopyrrolidin-1'-yl)- 4-oxo-1,8-naphthyridine-3-carboxylic acid and its salts;

1-(2,4-Difluorophenyl) -6-fluoro-1, 4-dihydro-7-{(1 α ,5 α ,6 α)-6-amino-N-benzyl-3-azabicyclo [3.1.0]hex-6-yl}- 4-oxo-1,8-naphthyridine-3-carboxylic acid and its salts;

1-(2,4-Difluorophenyl)-6-fluoro-1,4-dihydro-7-(3',3'-dimethyl-4'-hydroxy piperdin-1'-yl)-4-oxo-1,8-naphthyridine-3-carboxylic acid and its salts;

35 (RS)-(±)-9-Fluoro-6, 7-dihydro-8-{4'-(L- α -aspartyl-oxy)piperidin-1-yl}-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid hydrochloride;

7H-Pyrido[1,2,3-de]-1,4-benzoxazine-9-fluoro-2,3-dihydro-3-methyl-10-(3'-ethyl 4'-

hydroxypiperidin-1'-yl)-7-oxo-6-carboxylic acid and its salts;

7H-Pyrido[1,2,3-de]-1,4-benzoxazine-9-fluoro-2, 3-dihydro-3-methyl-10- (3'-amino methyl-4'-

hydroxypiperidin-1'-yl)-7-oxo-6-carboxylic acid and its salt;

5 1-Cyclopropyl-6, 8-difluoro-5-methyl-1, 4-dihydro -7-(3', 3'-dimethyl-4'-ethylamino piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salt;

1-cyclopropyl-6,7,8-trifluoro-5-methyl-1,4-dihydro - 4-oxo-quinoline-3-carboxylic acid.

(S)-(-)-9-Fluoro-6,7-dihydro-8- (3', 3'-dimethyl-4'-ethylaminopiperidin-1-yl)-5-methyl-1-oxo-1H, 5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts;

10 1-Cyclopropyl-6-fluoro-1, 4-dihydro-7- (3'-aminomethyl-4'-hydroxypiperidin 1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro-7- (4'-dimethylamino-3'-methylpiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-{4'-cyclopropyl aminopiperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1, 4-dihydro -7-(4'-(t-butoxycarbonyl (L)-Ala-Ala)amino-3', 3'-dimethyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid hydrochloride;

5-Amino-1-cyclopropyl-6-fluoro-8-methoxy-1, 4-dihydro -7-{4'-ethylamino-3', 5'-dimethylpiperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

Ethyl 1-(2,4-difluorophenyl) -6-fluoro -1, 4-dihydro-7- (4-amino-3-ethylpiperidin-1-yl)- 4-oxo-1,8-naphthyridine-3-carboxylate;

1-(2,4-difluorophenyl) -6-fluoro-1, 4-dihydro-7- (4-amino-3, 5-dimethylpiperidin-1-yl)- 4-oxo-1,8-naphthyridine-3-carboxylic acid and its salts;

Ethyl 1-(2,4-difluorophenyl) -6-fluoro-5-methyl-1, 4-dihydro-7- (4-amino-3, 3-dimethylpiperidin-1-yl)- 4-oxo-1,8-naphthyridine-3-carboxylate;

25 (S)-(-)-9-fluoro-6,7-dihydro-8- (4'-hydroxy- 3'-fluoropiperidin-1-yl)-5-methyl-1-oxo-1H, 5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts;

10-Fluoro-11- (4-aminopiperidin-1-yl)-3,4-dihydro-4 (S)-methyl-8-oxo-2H, 8H-pyrido[1,2,3-ef]-1,5-benzoxazipin-7-carboxylic acid and its salt;

30 (RS)-(±)-6, 7-dihydro-8- (trans-4'-hydroxy-3'-methylpiperidin-1-yl)-5-methyl-1-oxo-1H, 5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts;

(RS)-(±)-6, 7-dihydro-8- (cis-4'-hydroxy-3'-methylpiperidin-1-yl)-5-methyl-1-oxo-1H, 5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts; or

(RS)-(±)-6, 7-dihydro-8- (4'-hydroxy-3', 3'-dimethylpiperidin-1-yl)-5-methyl-1-oxo-1H, 5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts.

57. The method according to any one of claims 1, 4, 8, or 11 wherein the efflux pump inhibitor is selected from:

1-Ethyl-6-fluoro-1, 4-dihydro -7-(1', 2',3',4'-tetrahydroisoquinolin-2-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Ethyl-6, 8-fluoro-1, 4-dihydro -7-(4'-acetoxypiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Ethyl-6, 8-fluoro-1, 4-dihydro -7-(4'-{2'-(2'-oxazolidin-1-yl) ethyl} piperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Ethyl-6, 8-difluoro-1, 4-dihydro -7-((1 α ,5 α ,6 α)-6-amino-3-azabicyclo [3.1.0]-hex-3-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1- ethyl -6, 8-difluoro-1, 4-dihydro -7-(3'-amino-5'-methyl pyrrolidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1- ethyl-6, 8-difluoro-1, 4-dihydro -7-(4'-aminopiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1- ethyl -6, 8-difluoro-1, 4-dihydro -7-{4'-(acetamido) piperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1- ethyl-6, 8-difluoro-1, 4-dihydro -7-((1 α ,5 α ,6 α)-6'-(t-butoxycarbonyl amino)-3-azabicyclo [3.1.0]-hex-3-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro-7-(3'-acetamido-5'-methylpyrrolidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro-7-(3'-amino-5'-methylpyrrolidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1,4-dihydro--7-(4'-acetoxypiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1,4-dihydro -7-{4'-(dimethylamino) piperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1,4-dihydro-7-(3',5'-dimethylpiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro -7-(4'-hydroxy-3',5'-dimethylpiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro- -7-(3', 4', 5'-trimethyl piperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro- 7-(3', 5'-dimethyl-4'-ethyl piperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro-5-methyl- 7-(4'-ethoxypiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro-5-methyl- 7-(3', 3'-dimethylpiperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5 1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-{4'-(dimethylamino)-3'-methyl piperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-hydroxy-3'-isobutyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

10 1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-hydroxy-3',3'-dimethyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-hydroxy-3',5'-dimethyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(3'-methylpiperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5 5-Amino-1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(cis-4'-amino-3',5'-dimethylpiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6,8-difluoro-5-methyl-1,4-dihydro-7-(4'-hydroxy-3'-aminomethyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

20 5-Amino-1-cyclopropyl-6,8-difluoro-1,4-dihydro-7-(5'-amino-2'-methyl-pyrrolidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro -7-{3'-(L-Ala-L-Ala) amino pyrrolidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro -7-{4'-(di-n-butylamino) piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

25 5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro -7-{4'-(t-butoxycarbonyl-L-Ala-L-Ala)aminopiperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro -7-(4'- propionoxy piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

30 5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro -7-(4'-hydroxy-3',3'-dimethyl-piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6,8-difluoro-1, 4-dihydro -7-{4'-(1-pyrrolidinyl) piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6,8-difluoro-1,4-dihydro-7-{4'-[(piperidin-4-yl) aminomethyl]-piperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

35 5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro -7-{(1,2',2', 6',6'-pentamethyl piperidin-4-yl)methylamino}-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6,8-difluoro-1, 4-dihydro -7-(3',5'-dimethyl morpholin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro -7-(4'-cyclopropyl piperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5 5-Amino-1-cyclopropyl-6, 8-difluoro-1, 4-dihydro -7-(3', 5'-dimethyl-4-pivaloyl piperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

Ethyl 6,8-Difluoro-7-(4-hydroxypiperidin-1-yl)-1-(1-phenylthio-3(*S*)-but-3-yl)-1,4-dihydro-4-oxo-quinoline-3-carboxylate;

10 1- (2'-Trifluoromethylphenyl) -6-fluoro-1, 4-dihydro- -7-(3', 3', 4'-trimethyl piperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1- (2'-trifluoromethylphenyl)-6,8-difluoro-1, 4-dihydro -7-(morpholin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1- (2'-trifluoromethylphenyl) -6, 8-difluoro-1, 4-dihydro -7-(3',5'-dimethylmorpholin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5 5-Amino-1- (2'-trifluoromethylphenyl) -6, 8-difluoro-1, 4-dihydro -7-(3',5'-dimethyl piperazinyl-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1- (4'-trifluoromethylphenyl) -6, 8-difluoro-1, 4-dihydro -7-(3'-aminopyrrolidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

20 1- (4'-Fluorophenyl) -6-fluoro-1,4-dihydro -7-{4'-ethylamino)piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1- (2',4'-Difluorophenyl) -6-fluoro-1, 4-dihydro-7-(3', 5'-dimethyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1- (2',4'-difluorophenyl) -6, 8-difluoro-1, 4-dihydro -7-(3'-hydroxy-5'-methylpyrrolidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

25 5-Amino-1- (2',4'-difluorophenyl) -6, 8-difluoro-1, 4-dihydro -7-(3',3'-dimethyl piperazinyl-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro -7-[(3'-aminoethoxycarbonyl)pyrrolidin-3-yl]-4-oxo-naphthyridine-3-carboxylic acid and its salts;

30 1-Cyclopropyl-6-fluoro-1,4-dihydro-7-(pyrrolidin-3-yl-amino)-4-oxo-naphthyridine-3-carboxylic acid and its salts;

1- (2',4'-Difluorophenyl) -6-fluoro-1, 4-dihydro -7-(piperidin-4-yl-amino)-4-oxo-naphthyridine-3-carboxylic acid and its salts;

Ethyl-1- (2',4'-difluorophenyl) -6-fluoro-1, 4-dihydro -7-[[1 α ,5 α ,6 α]-3-N-benzyl-3-azabicyclo[3.1.0]hex-6-yl-amino}-4-oxo-naphthyridine-3-carboxylate and its salts;

35 1-(2,4-difluorophenyl) -6-fluoro-7-(1-phenyl-4,5,6,7-tetrahydropyrazolo [4,3-c]pyridin-1-yl-1, 4-dihydro-4-oxo-1, 8-naphthyridine- 3-carboxylic acid and is salts;

(S)-(-)-9-Fluoro-6,7-dihydro-8-(4'-carboxamidopiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts;

(R)-(+)-9-Fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid L-arginine salt;

5 (S)-(-)-9-Fluoro-6,7-dihydro-8-(4'-hydroxy-3',3'-dimethylpiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts;

(S)-(-)-N-methylpiperidin-1-yl-9-fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylate;

10 (S)-(-)-Morpholinoethyl-9-fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylate and its salts;

Ethoxycarbonylmethyl (R)-(+)-9-fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylate;

N-1-{7-(1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid)}-N-3-amino-{7-(1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid)}-pyrrolidine;

N-1-{7-(1-cyclopropyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid)}-N-3-amino-{7-(1-cyclopropyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid)}-pyrrolidine;

20 N-1-{7-(1-cyclopropyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid)}-N-3-amino-{7-(1-cyclopropyl-6,8-difluoro-5-amino-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid)}-pyrrolidine;

N-1-{7-(1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid)}-N-4-{7-(1-cyclopropyl-6,8-difluoro-5-amino-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid)}-piperazine;

25 N-1-{7-(1-cyclopropyl-6-fluoro-5-methyl-1,4-dihydro-4-oxo-quinolone-3-carboxylic acid)}-N-3-amino-{7-(1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid)}-pyrrolidine;

N-1-{7-(1-cyclopropyl-6-fluoro-5-methyl-1,4-dihydro-4-oxo-quinolone-3-carboxylic acid)}-N-4-amino-{7-(1-cyclopropyl-6,8-difluoro-5-amino-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid)}-piperidine;

30 N-1-{7-(1-cyclopropyl-6-fluoro-5-methyl-1,4-dihydro-4-oxo-quinolone-3-carboxylic acid)}-N-3-amino-{7-(1-cyclopropyl-6,8-difluoro-5-amino-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid)}-pyrrolidine;

N-1-{7-(1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid)}-N-4-{7-(1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid)}-

35 piperazine;

N-3-azabicyclo{7-(1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid)}-[1 α ,5 α ,6 α]-N-6-amino-{7-1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid)}-[3.1.0] hexane; or
N-1- {7-(1-cyclopropyl-6,8-difluoro-5-amino-1, 4-dihydro-4-oxo-quinolone-3-carboxylic acid)}-N-4-amino-{ethyl 2,3,6-trifluorophenyl-4-carboxylate}-piperidine.

58. The method according to any one of claims 1, 4, 8, or 11 wherein the efflux pump inhibitor is selected from:

1-Cyclopropyl-6-fluoro-1, 4-dihydro-5-methyl- 7-(4'-methoxypiperidin -1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

7-Bromo-1-cyclopropyl-6-fluoro-5-methyl-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1, 4-dihydro -7-(4'-amino-3'-methylpiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-amino-3'-methyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro -7-{3,3-dimethyl-4'-ethylamino piperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-amino-3'-3'-dimethyl piperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-{4'-(dimethylamino)piperidin-1-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(4'-hydroxy-4'-methylpiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-7-(3',3'-dimethyl-4'-hydroxypiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6,8-difluoro-5-methyl-1,4-dihydro-7-(3'-aminomethyl-4'-hydroxypiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6,8-difluoro-1,4-dihydro-7-(3'-aminomethyl-4'-hydroxypiperidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Ethyl-6,8-difluoro-1,4-dihydro-7-(3'-5'-dimethylpiperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1,4-dihydro-7-(4'-ethyl-3'-methylpiperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1,4-dihydro-7-(3'-5'-dimethyl-4'-ethylpiperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

1-Ethyl-6, 8-difluoro-1, 4-dihydro -7- $\{(1\alpha,5\alpha,6\alpha)-6'$ -amino-3'-azabicyclo [3.1.0] hex-3'-yl}-4-oxo-quinoline-3-carboxylic acid and its salts;

5 5-Amino-1-(2',4'-difluorophenyl)-6,8-difluoro-1,4-dihydro-7-(3'-aminopyrrolidin-1-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

5-Amino-1-cyclopropyl-6,8-difluoro-1,4-dihydro-7- $\{(3'$ -aminoethoxycarbonyl pyrrolidin-3-yl)-4-oxo-quinoline-3-carboxylic acid and its salts;

10 1-Cyclopropyl-6-fluoro-1,4-dihydro-7-(pyrrolidin-3'-ylamino)-4-oxo-naphthyridine-3-carboxylic acid and its salts;

1-(2',4'-Difluorophenyl)-6-fluoro-1,4-dihydro-7-(piperidin-4'-ylamino)-4-oxo-naphthyridine-3-carboxylic acid and its salts;

1-Cyclopropyl-6-fluoro-1, 4-dihydro -7-(4'-amino-3'-ethylpiperidin-1-yl)-4-oxo-naphthyridine-3-carboxylic acid and its salts;

5 (S)-(-)-9-Fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid 0.2 hydrate;

(S)-(-)-9-Fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid . choline salt;

20 (S)-(-)-9-Fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid. 1-Hydroxyethylpyrrolidine salt.

(S)-(-)-9-Fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid. Diethanolamine salt;

(S)-(-)-9-Fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylate. L-histidine salt;

25 (RS)- (\pm) -9-Fluoro-6,7-dihydro-8- $\{4'-(D\text{-phenylalanyloxy})$ piperidin-1-yl}-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid hydrochloride;

(RS)- (\pm) -9-Fluoro-6,7-dihydro-8- $\{4'-(L\text{-}\alpha\text{-aspartyl oxy})$ piperidin-1-yl}-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid hydrochloride;

30 (\pm) -9-Fluoro-6,7-dihydro-8- $\{4'-(L\text{-leucyl oxy})$ piperidin-1-yl}-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid dihydrochloride;

(-)-9-Fluoro-6,7-dihydro-8- $\{4'-(D\text{-leucyl oxy})$ piperidin-1-yl}-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid hydrochloride;

(S)-(-)-9-Fluoro-6,7-dihydro-8- $\{4'-(L\text{-alanyloxy})$ piperidin-1-yl}-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid hydrochloride;

35 (S)-(-)-Morpholinoethyl-9-fluoro-6,7-dihydro-8-(4'-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylate and its salts;

(R)-(+)-8,9-difluoro-6,7-dihydro-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2- [S-phenylalanyl-S-lysine methyl ester]carboxamide;

(RS)-(±)-9-Fluoro-6,7-dihydro-8-(trans-4'-hydroxy-3'-methylpiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts;

5 **(RS)-(±)-9-Fluoro-6,7-dihydro-8-(cis-4'-hydroxy-3'-methylpiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts;**

(S)-(-)-9-Fluoro-6,7-dihydro-8-(trans-4'-hydroxy-3'-methylpiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid and its salts;

10 **7H-Pyrido[1,2,3-de]-1,4-benzoxazine-9-fluoro-2,3-dihydro-3-methyl-10-(4'-hydroxy-3'-ethylpiperidin-1'-yl)-7-oxo-6-carboxylic acid and its salts;**

10-Fluoro-11-[(1 α ,5 α ,6 α)-6-amino-3-azabicyclo[3.1.0]hex-3-yl]-3,4-dihydro-4(S)-methyl-8-oxo-2H,8H-pyrido[1,2,3-ef]-1,5-benzoxazepine-7-carboxylic acid. Hydrochloride.